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# BULLETIN

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# THE JOHNS HOPKINS HOSPITAL

Entered as Second-Class Matter at the Baltimore, Maryland, Postoffice
Acceptance for mailing at special rate of postage provided for in Section 1103, Act of October 3, 1917. Authorized on July 3, 1918.

Vol. XXX—No. 335] BALTIMORE, JANUARY, 1919 [Price, 50 Cents


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## CLINICAL OBSERVATIONS ON EPIDEMIC INFLUENZA[1]


By Arthur Bloomfield and George A. Harrop, Jr.

*(From the Medical Clinic of The Johns Hopkins Hospital)*


During the recent epidemic of influenza, about 300 cases of the disease were admitted to The Johns Hopkins Hospital. Inasmuch as most of the patients were seen from the very onset of symptoms and went through their illness without complications, an unusual opportunity was afforded to study the clinical features of the entire course of the disease. The material was drawn from certain limited groups of individuals, to wit:

The nursing staff of the hospital (about 350 in number), living in the nurses' home.

The medical students (about 400 in number) quartered in boarding houses and clubs.

The hospital physicians (about 100 in number), residing mainly in the hospital.

The hospital service staff (about 200 in number), living mainly in the domestic home of the hospital or in the nurses' home.

Eight cases arose among the patients in the public wards and a few more were admitted as emergencies from various parts of the city.

Of the entire group, about 300, or approximately 30 per cent, developed the disease; of the nurses, nearly 40 per cent fell ill.

[1] Read before The Johns Hopkins Hospital Medical Society, November 18, 1918.

The main statistical facts of the epidemic are summarized in the following table and chart, which are based on the study of 268 patients admitted between September 24th and October 20th.

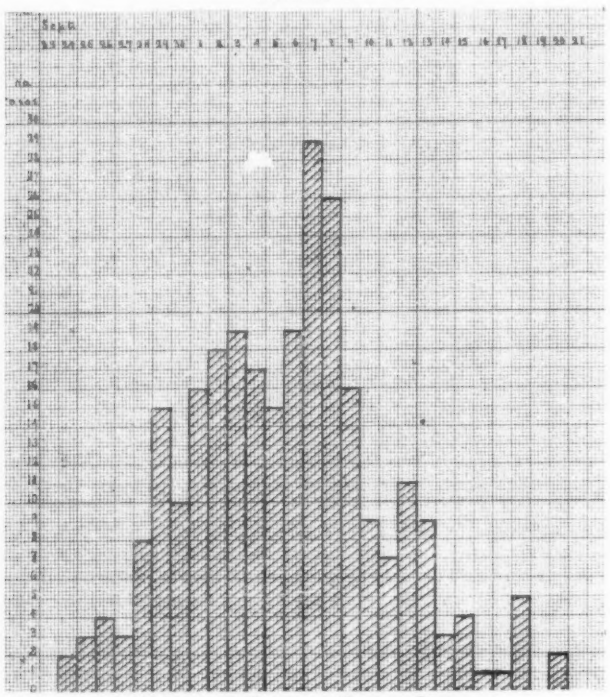
TABLE I

General Statistics of the Influenza Cases in The Johns Hopkins Hospital

| | No. | Per Cent |
|---|---|---|
| Total cases | 268 | |
| Total deaths | 13 | 4.8 |
| Total number developing pneumonia | 41 | 15.3 |
| Total deaths among pneumonia patients | 13 | 32.0 |
| Total deaths among patients in hospital from start of disease | 7 | 2.7 |
| Total number of patients in hospital from start of disease developing pneumonia | 28 | 11.0 |
| Total number of patients admitted with frank pneumonia | 13 | |
| Total deaths among patients admitted with pneumonia | 6 | 46.0 |
| Total deaths among patients developing pneumonia in the hospital | 7 | 25.0 |
| Total number of nurses admitted | 123 | |
| Total number developing pneumonia | 12 | 9.8 |
| Total deaths | 3 | 2.4 |
| Total deaths of patients developing pneumonia | 3 | 25.0 |

Chart I illustrates graphically the course of the epidemic. The rapid rise following the few preliminary cases, and the sudden drop after the height of the epidemic was reached, correspond with the curves of previous epidemics. With the sudden falling off in the number of cases there was a remarkable change in the clinical character of the disease. The fulminating type was no longer seen, the patients were much less ill, the erythema of skin and mucous membranes was slight or absent, pneumonia was much less frequent, and in general the picture approximated closely that seen in "influenza nostras," or "endemic grippe." All the patients who died fell ill before October 10th.

CHART I



NUMBER OF CASES BY DAY OF ONSET.

The appearance of the epidemic made necessary a rapid reorganization of the hospital, in order to handle the increasing number of cases. This was made possible by the efficient activities of the superintendent's office and of the superintendent of nurses. The disposition of the patients was planned with the idea of preventing secondary epidemics of pneumonia. Not more than thirty patients were housed in one ward, the rows of beds were single, and screens were placed between every two beds. Each patient had a separate thermometer, and all linen, utensils and dishes were boiled after use. Paper towels, handkerchiefs and sputum cups were burned. The patients were instructed to cover the mouth when coughing, and all attendants wore gowns and gauze masks (4 to 8 thicknesses) while in the wards. As soon as pneumonia or any other complication developed, the patient was specially isolated in a separate room.

Each block of twenty to forty cases was in charge of an interne, assisted by one or more fourth-year medical students. They took the histories, made the notes, carried out the laboratory tests, and had charge of the immediate needs of the patients. The resident and assistant resident exercised systematic supervision over the wards, and the physician-in-chief consulted in the severe cases and advised generally in the conduct of the epidemic. Admission of patients was done by a set of externes rapidly trained in the diagnosis of influenza. Throughout the entire epidemic no case of another infectious disease was admitted to the influenza wards. The organization of the "influenza staff" would have been ideal had it not been necessary constantly to replace men stricken down by the disease. Thus, by the end of the epidemic the entire staff except three members had been renewed by successive substitutes.

It was found necessary to schematize in the handling of the patients, owing to the tremendous nursing problem. A set of routine orders for influenza cases was therefore worked out, which applied automatically to all patients. These orders covering the main needs of most patients were supplemented by any special directions necessary. Another routine was worked out for the regulation of the patients' activity during convalescence. This was found satisfactory in practically all the uncomplicated cases, and saved much labor for the ward staff. No medical or scientific books, or newspapers, were allowed in the wards. It was thought that the harrowing accounts of the epidemic in the latter might have a bad effect on patients already depressed.

The routine study of the case consisted of a history uniformly taken to cover in detail such questions as exposure and onset symptoms, a complete and thorough physical examination, a leucocyte count on admission, and at intervals until discharge, blood pressure on admission and discharge, urine examination on admission, repeated if abnormal findings were present, and two-hourly observations of temperature, pulse and respiration. Frequent detailed notes were made by the internes and staff on the course of the disease and its special features.

## CLINICAL OBSERVATIONS

The material furnished an unusual opportunity to study the early stages of the disease, since about one-half of the cases were drawn from a closed group of individuals—namely, some 350 nurses residing in The Johns Hopkins Nurses' Home. At the start of the epidemic it was hoped that extensive spread among the nursing staff might be prevented by early detection and isolation. Communication between this group and the outside world was, therefore, almost completely cut off, and they came in contact only with each other, with the staff, and with the patients in the wards. Furthermore, they were instructed to report for observation at the first symptom of any sort. Practically all the cases, therefore, were seen from the very start, and it was possible to study in detail the earliest symptoms and the mode of onset. From these ob-

servations, it was clearly apparent that the disease is not primarily a local respiratory infection, and that it presents a clean-cut, definite clinical picture, quite independent of pulmonary complications. It should also be emphasized that influenza, as seen now, corresponds in detail with the descriptions of the previous pandemics—it is undoubtedly the same disease

The disease is ushered in by two groups of symptoms; in the first place the constitutional reactions of an acute febrile disease—headache, general aching, chills, fever, malaise, prostration, anorexia, nausea or vomiting; and in the second place, symptoms referable to an intense congestion of the mucous membranes of the nose, pharynx, larynx, trachea, the upper respiratory tract in general, and of the conjunctivæ. Superficially, the onset seems to vary in different cases, depending on whether one or the other of these sets of symptoms predominates, but a striking essential similarity prevails, which is most obvious during the height of the epidemic, when the disease runs more constantly true to type. For this reason it seems misleading to divide the ordinary run of cases into respiratory, abdominal and nervous. It would seem better to reserve the last term for those patients showing organic lesions of the nervous system or psychoses more outspoken than the usual temporary depressions.

Three distinct types of invasion were noted—abrupt invasion, gradual invasion and invasion with intermittent symptoms. The departure from health was extremely sudden in many of the cases, especially the severe ones at the height of the epidemic, definite symptoms beginning after only a few hours of vague malaise. In some cases the patient was knocked flat, literally dropping in his tracks. The most common symptoms were sudden and marked malaise and prostration, chills or chilly sensations, intense headache and general aching, pain in the eyes and photophobia. In a few instances, acute abdominal pain, vomiting or diarrhea ushered in the disease. In these severe cases the temperature usually rises rapidly, reaching its height within 24 hours. Coincident with, or shortly following onset, as the hyperemia of the mucous membranes develops, there is dryness, tightness, fullness, or slight rawness of the throat, substernal discomfort, and tight, racking cough, without sputum. There may be stoppage of the nose from swelling of the mucous membrane, with slight watery nasal discharge, and conjunctivitis is practically always present. The remarkable flushed appearance of the face and buccal cavity to be described below is usually fully developed in twenty-four hours. In another large group of cases the invasion is gradual, the symptoms unfolding themselves over a period of one to three days before the disease becomes full blown. It is in this group that isolated symptoms, such as headache, sore eyes, "coryza," raw throat, dry cough, anorexia, insomnia, or pain in the back may for a time predominate, masking at first the essential identity of all the cases. During such a period of invasion the temperature is usually normal, or only slightly elevated. In the early part of the epidemic, we observed many cases of this sort for two or three days, uncertain as to the diagnosis, until sudden high fever and frank symptoms and signs made the condition obvious. In a third group of cases the early symptoms were very puzzling, because of their intermittent nature. Thus, headache and malaise might be present one day and gone the next. Nausea might then come on for a few hours, again leaving the patient feeling well. After alternating periods of minor symptoms and well-being, lasting for several days, the full-blown disease finally made its appearance.

Of particular interest were certain symptoms that were present within the two weeks preceding the onset, but which apparently were independent of the actual disease. Such phenomena were noted in 36 instances; for example, S. had headache and a cold for two weeks, and H. had slight cough and occasional malaise for five days before onset. M. had coryza which cleared up two days before onset, K. had sore eyes and photophobia for a week, and N. had "coryza earlier in the week, which had practically subsided at onset." C. had been nervous and restless for four days, and J. had had a cough for two weeks before onset. In general, these "pre-onset" symptoms were in the nature of mild upper respiratory tract disturbances of from one to two weeks' duration, usually improving or well at the time of definite onset of the influenza.

*Physical Examination.*—Although evidence of gross lesions is absent in uncomplicated cases, the physical findings are none the less clean-cut and typical. The general appearance is most striking. In well-marked cases, there is an intense, dusky, reddish-plum-colored erythema of the face, lips and upper chest, which usually fades off abruptly at the level of the breast, but may extend over the entire chest and back, and occasionally involves the arms and legs. The entire facies has a remarkable suffused look, not unlike that seen in polycythemia vera. It is, however, quite different from true cyanosis, and studies of the oxygen-combining capacity and content of the blood in these patients gave normal results. The color blots out on pressure, returning instantly. In milder cases this tint is at times less striking, but it was present to some degree in practically all, and even where not obvious, a faint purplish erythema could be demonstrated by pressure. The peculiar dusky appearance of the face often persisted for weeks into convalescence, quite independent of transient flushing on exertion, which accentuated the underlying hue. In seven cases a fine, branny desquamation was noted over face and upper chest. Conjunctivitis was often very marked, with lachrymation and photophobia.

Early in the course of the epidemic we noticed an unusual bright red appearance of the throat in most of the patients, and more careful study of subsequent cases showed this to have striking and constant features. The changes in the mouth usually become full-blown during the first twenty-four hours of the disease. The most striking feature is a bright vermilion or scarlet injection of the pharynx, tonsils, pillars and soft palate. In many cases, this erythema extends over the entire mouth, and can be exquisitely demonstrated by pressure on the mucosa of the cheek with a spatula. In the

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most marked cases, the entire mouth cavity has a flaming appearance. On analysis, this redness is seen to be due to a diffuse hyperemia of the mucous membrane, together with an injection of minute blood vessels on the pharynx and pillars, but especially on the soft palate. There is a line of demarcation at the hard palate, which is relatively free. In some cases, especially the mild ones, these changes are less marked, being confined to the soft palate and pillars. There is extreme swelling of the lymphoid tissue of the posterior pharyngeal wall, which gives it a remarkable corrugated appearance. These changes are clearly in the nature of an erythema, and there is never any localized exudate (Fig. 1).

The tongue is usually coated, but if clean is bright red like the buccal mucosa.

In from one-half to two-thirds of the cases at onset, one to three or four, or even more, dark, crimson spots were seen on the mucosa of the inside of the cheek (Fig. 2). They were occasionally present on the gums, soft palate, mucous border of the lips, or on the uvula. These spots vary from a minute pin-point up to one millimeter in diameter, and may be arranged in one or more clusters. The dark cherry color and sharp margin characterize them and seem to indicate that they are of hemorrhagic origin. The individual spots fade rapidly, disappearing without trace in from one to two days. They may reappear in repeated crops in the same individual, and are seen in convalescence in most of the cases. About 94 per cent of our patients in whom they were systematically looked for showed them at some time during the course of the disease.

Inasmuch as we had never observed such spots before, and were unable to find any account of them in the literature, it appeared at first as if they might be specific of influenza as Koplik's spots are specific of measles. After the epidemic, however, it was possible to examine several hundred mouths of individuals who had had no symptoms of influenza, and in them also these spots were frequently present. In 303 examinations of 55 controls made daily over a period of one to nine days, the spots were seen 110 times, or in 36.6 per cent. They were seen at some time in 84.2 per cent of 38 controls examined daily over a period of a week or more. It was striking, however, that the spots were usually much smaller and less bright than in the influenza patients. Although they are obvious and often picturesque in the latter, they are frequently so insignificant in the controls that they are found only on careful search. Possibly the hyperemia of the mouth in influenza presents a specially favorable condition for their development. Their exact cause is uncertain; they may be due to slight trauma to the mucosa of the mouth. So that although these spots are not a specific lesion, their presence in typical form may have a certain degree of clinical specificity.

Another striking feature in the appearance of the mouth was a swelling of the minute nodules normally present on the soft palate. They were often extremely prominent, appearing as white or gray glistening, rounded bodies, varying in size from 1 to 3 millimeters in diameter. They were usually abundant, the entire soft palate being thickly seeded with them, and they stood out sharply against the surrounding hyperemia.

In summary, then, the mouth presents a very striking picture, which seems distinctly characteristic. Although, most writers have noted that the throat is injected, the observation by Tigri,[2] in 1867, now lost in obscurity, is the only one we have found which describes a typical enanthem. Tigri noted the peculiar injection of the soft palate, and likened it to the enanthem of measles.

The general appearance of the mouth may remain full-blown for about a week. The erythema then fades, usually leaving a striking capillary injection of the soft palate and pillars. In some cases, the redness of the entire mouth persisted for several weeks into convalescence.

Herpes was noted in nine per cent of the cases. In a few, it was present at onset, but might appear at any time during the active stage of the disease. It was no more frequent in the pneumonias than in the uncomplicated cases. There are no striking cardiovascular features; the pulse is usually only slightly accelerated, and the blood pressure tends to be subnormal. Abdominal examination is essentially negative. The spleen was felt in only three cases. Unless complication sets in, the lungs are clear, although a few transient crackles could at times be heard over the lower lobes at the beginning of the examination. Minor skin rashes were noted in 10 cases. A few erythematous papules on the chest and shoulders or a few small petechiæ were seen. Three patients had transient urticarial eruptions, and one a generalized morbilliform rash. In general, apart from the erythema, the skin changes are insignificant.

*Course of the Disease.*—Once fully established, the disease picture was remarkably constant. The fever usually continued high for from three to eight or nine days, with morning drops, the constitutional symptoms persisting until the temperature began to fall. At this time, particular discomfort, such as headache, backache, nausea, etc., gradually or suddenly disappeared, giving place to a profound feeling of collapse or exhaustion. The tight, racking cough often increased after the first day, with the production of more or less whitish, yellowish or greenish mucoid sputum, which in some cases persisted for weeks into convalescence. This is a regular feature of the disease, but other respiratory tract involvements must be regarded as complications. Some of the cases ran their whole course without cough, sputum or respiratory symptoms. Epistaxis was noted in 10 per cent of the patients. It occurred at onset, or at any time during the active stage, and in a few cases there were repeated epistaxes. This bleeding is doubtless associated with the hyperemic condition of the nasal mucosa. Nearly all the more severe cases had marked anorexia or nausea. The feeding problem became very difficult, and even fluid was

[2] Tigri: *Omodei annali di medicina*, Milan, 1867, CCII, 67.

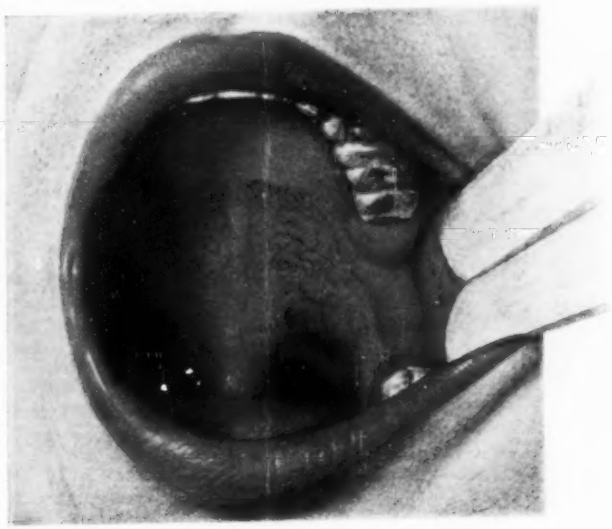


FIG. 1.

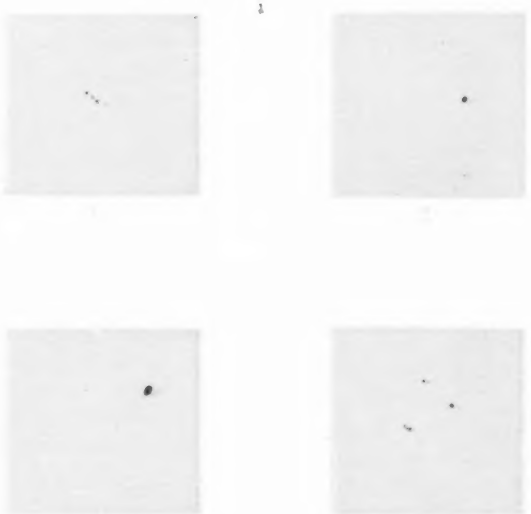


FIG. 2.

refused. Stubborn constipation was the rule, although a few patients had brief attacks of diarrhea. In no other disease does one see such constant lack of cheer in the patients' faces. Nothing satisfies them, they are extremely unhappy and gloomy, and seem to feel that things can never be normal or comfortable again. Pathological depressions were, however, strikingly absent in our cases.

*Convalescence.*—The classical post-influenzal asthenia described in previous epidemics was noted in these cases. Profound prostration persisted for weeks into convalescence. The patients for the most part feel fairly comfortable while lying flat in bed, but the slightest exertion is followed without warning by exhaustion, a feeling of collapse, sweating and palpitation. Apart from actual physical weakness, which is marked, they complain of an intensely disagreeable sensation, which may be best characterized as an extreme lack of well-being, rather than any positive pain or discomfort. This state of affairs usually persisted as long as the patients were under observation—about three or four weeks. Physical examination during convalescence is essentially negative. Tachycardia and sinus arrhythmias or extrasystoles are common, and in many cases the racking cough, with more or less mucoid or mucopurulent sputum persists. Anorexia, headache and insomnia were frequent complaints and loss of weight up to 20 pounds was not uncommon.

*Mild, Abortive and Atypical Cases.*—These were of particular interest from an epidemiological and diagnostic standpoint. During the course of the epidemic about 20 cases were observed with such slight symptoms and signs that the presence of any definite disease was doubted. It was only at the end of about a week, when typical prostration appeared, that the diagnosis was made certain. Many patients did not apply for medical aid until this period of the disease, presenting as cases of tachycardia, insomnia or general breakdown. They furnished the key to a still larger group of very mild or abortive cases, which indicate clearly that the total number of individuals affected is much greater than the number of manifest cases. In some of these individuals with practically no symptoms, the diagnosis was clinched by the typical appearance of the throat or by an extreme leucopenia.

Of the patients admitted to the wards, 30 ran an afebrile course, although there was usually some abnormality of the temperature curve. These were by no means the mildest cases; on the contrary, many who came down with sharp reactions recovered more promptly and were less prostrated.

## Laboratory Examinations

*Urine.*—In the severer cases, a febrile albuminuria was present, usually clearing up promptly after free intake of water. No permanent renal disturbance was noted. The patients with pneumonia showed large amounts of albumin and casts.

*Blood Pressure.*—The blood pressure was either normal or low. Low readings were especially frequent in the very asthenic cases. Systolic pressures of 80 to 100 mm. Hg., and diastolic pressures as low as 50 were common. In convalescence, the pressures were essentially normal.

*Leucocytes.*—Leucopenia was the rule during the active stage of the disease. The average counts on the first or second day were about 4000 to 5000, but they varied from 2000 up to normal numbers in different cases. The low count persisted into convalescence, usually returning to normal during the third or fourth week. In some cases the normal mark was overshot, the count rising to 12,000 to 15,000—occasionally even higher. Differential counts during the stage of leucopenia usually show an absolute decrease of polymorphonuclears, with relative lymphocytosis. In some cases, the lymphocytes were absolutely decreased as well. It was of interest that many mild cases had extremely low counts, and that the leucocyte curves seemed unaltered by the occurrence of complicating bronchopneumonia.

## Temperature Curves

Temperature readings were taken every two hours throughout the acute stage. In Table II is summarized the day of the disease on which the temperature became normal. It is apparent that this is not a three-day fever. Even in uncomplicated cases, the pyrexia usually lasts from five to nine days. From a study of complete temperature curves obtained in cases developing in the wards, it was possible to determine the details of the entire course of the fever. The following general statements may be made:

TABLE II

THE DURATION OF THE FEVER ACCORDING TO THE DAY OF DEFERVESCENCE, AND THE NUMBER OF CASES

Temperature became normal on—

| Day of Disease | Number of Cases |
|---|---|
| 1 | 0 |
| 2 | 0 |
| 3 | 7 |
| 4 | 15 |
| 5 | 25 |
| 6 | 24 |
| 7 | 44 |
| 8 | 28 |
| 9 | 22 |
| 10 | 6 |
| 11 | 4 |
| 12 | 1[a] |
| | 176 |

[a] Bronchopneumonia?

In 30 cases there was no fever during the hospital stay.

1. The temperature rises gradually at onset, rarely reaching its height in less than 24 hours.

2. Fever continues for a variable period, falling gradually in about one-half the cases, and suddenly (in 24-36 hours) in the remainder.

3. There is rarely a steady fastigium, the morning temperature usually being from one to three degrees lower than the evening reading.

4. After falling, the temperature may remain normal, it may be subnormal for several days, or there may be slight post-febrile rises.

5. Secondary rise of fever usually indicates a complication, but such rise may occur in uncomplicated cases.

6. An occasional chart may show an entirely bizarre, non-uniform curve.

7. Some charts show only slight elevations throughout the course.

8. The pulse is usually relatively slow, but follows the temperature curve in a general way.

It appears, therefore, that while the temperature curves vary in character, the fever is one of distinctly determinate duration. In 95 per cent of the cases the temperature reached normal by the ninth day, and in no uncomplicated case did it persist beyond the eleventh day. Some of the main features of the fever are shown in the appended charts.

### Complications

Apart from the pneumonias, which occurred in 41, or 15.3 per cent of the cases, complications were few. Mild sinus infections occurred in two cases, catarrhal otitis media in six, while one patient developed an acute mastoiditis requiring operation. Laryngitis giving frank symptoms occurred three times.

A group of 19 patients was of particular interest. They developed localized patches of fine, crackling rales, with some impurity of breath sounds over one or both lobes. These signs usually appeared at the height of the disease and persisted for a few days to several weeks. A beginning pneumonia was naturally suspected, but in no case was there bloody sputum, respiratory symptoms, or any unusual rise of temperature. The normal course of the disease seemed unaltered. X-rays made in several of these cases showed no localized shadow.

### Epidemiological Observations

Despite the striking general facts in regard to the gross spread of the disease, the details of contagion and infection are quite obscure. We desire to put on record certain observations which seem of interest, without attempting to draw any definite conclusions.

The disease is contagious during the incubation period. E. visited his sister who was at a country place where no influenza had appeared. He was there for a few hours in the morning. On his arrival in Baltimore six hours later, symptoms appeared. He had a severe type of the disease, with secondary pneumonia of which he died on the eighth day. Two days after contact the sister developed a severe case of influenza. Family H. were in the country with no influenza in the vicinity. Mrs. X. and her son came to visit them. A day or so later, the boy developed the disease. H., who is a physician, sent mother and boy away at the onset of symptoms, but three days later his own three children developed severe attacks. These observations are also in harmony with the generally accepted idea that the incubation period is about two days.

Medical student B. came to Baltimore with the disease full-blown. His room-mate slept in the same bed with him for two nights, but did not develop influenza. Most of the nurses are quartered two in a room. Among 150 of them who developed influenza, there were only 12 pairs of room-mates. Except in the case of three pairs, each of the two came down within two days of the other. This perhaps indicates that infection took place mainly before symptoms were well developed, when the nurses were in general contact in the assembly rooms and dining hall. General use of gauze face masks in the wards did not seem to alter the course of the epidemic. If these masks are protective, infection from early unisolated cases must be assumed.

Only eight of the patients in the general public wards developed influenza, although 40 per cent of the attendants were affected; and numerous individuals did not contract influenza until they had been constantly exposed for as long as two weeks.

These observations are of interest in so far as they confirm facts noted in previous epidemics, and indicate our total lack of insight into the details of the mode of infection and spread of the disease, apart from the gross fact of its extreme contagiousness.

### Etiology

A consideration of the etiology of influenza must include a discussion of two questions. Is the influenza bacillus the cause of the disease, and if not, what is the etiological agent? The main evidence in favor of the Pfeiffer bacillus' being the cause of influenza is the observation that in certain localities it has been isolated from the respiratory passages in a large percentage of the cases. Against its etiological nature, several facts may be noted: Apart from the presence of the organism, no definite relation to the uncomplicated disease by isolation from a specific lesion, or development of immunity reaction, has been proved. Neither experimentally in animal or in man has influenza or a condition simulating it been produced by inoculation with cultures of the influenza bacillus. The influenza bacillus is present in interepidemic times in the nasopharynx of normal persons, and in a large percentage of acute and chronic respiratory infections. Luetscher, for example, in 603 sputum cultures, isolated the influenza bacillus in pure culture from 28.5 per cent of cases of non-tuberculous infection. The organism is essentially symbiotic with other bacteria, both *in vivo* and *in vitro*. It is well known that it grows much better in the presence of other bacteria, such as staphylococci, giving rise to so-called giant colonies. In isolating pneumococcus from sputum by mouse inoculation, the influenza bacillus commonly comes through into the animal's blood with the pneumococcus, while other organisms remain localized in the peritoneum. Sputum cultures from cases of lobar pneumonia may yield *B. influenzæ* in pure or almost pure culture, where the lung puncture shows only pneumococcus, indicating the tendency

of the organism to press in wherever other bacteria are present. The influenza bacillus has been found in tonsils, inflamed and normal, in pleurisy, in sinus and middle ear infections, in the entire respiratory tract from nose to alveoli, in bronchiectases, in the urinary tract, in the meninges, and in association with tuberculosis, diphtheria, measles and scarlet fever. In these conditions, the rôle of the influenza bacillus, while superficially prominent, is clearly not fundamental.

Bacteriological studies, made in our cases by Dr. Howard, which are reported in detail elsewhere, did not bring evidence that the bacillus of Pfeiffer is the cause of epidemic influenza. Blood cultures made at onset in the acute cases were uniformly negative, and it was only in the terminal stage of the complicating pneumonias that organisms appeared in the blood. Pneumococcus or streptococcus was isolated in a few instances, but no influenza bacilli. Naso-pharyngeal swabs made at onset showed the usual mouth flora. Gram-negative bacilli were seen in smears in some of the cases, but only once as the predominating organism. In three instances of post-influenzal pneumonia, the Pfeiffer bacillus predominated in the sputum culture, but in most cases the pneumococcus, green streptococcus and other organisms were mainly present.

Similar bacteriological findings which are now being reported by other observers cast doubt on the rôle of the Pfeiffer bacillus as the primary cause of uncomplicated epidemic influenza; it is probable that the actual virus is as yet unidentified. It is of interest, however, to point out some striking analogies between this disease and certain of the acute exanthemata, especially measles. They are both extremely contagious. They both tend to break out in epidemic form from time to time, but sporadic cases persist between epidemics. Each has an incubation period of strikingly constant length and a febrile reaction of determinate duration. They both have characteristic leucocytic changes. The uncomplicated cases all show striking absence of gross lesions. In both diseases these are hyperemic phenomena of the skin and throat, and a remarkable tendency to complications, especially in the respiratory tract. It should, however, be strongly emphasized that there is no evidence of any actual relationship between these two diseases.

## CONCLUSIONS

The observations herewith presented may be summarized as follows:

1. Epidemic influenza in 1918 is clinically identical with the disease as seen in previous pandemics.

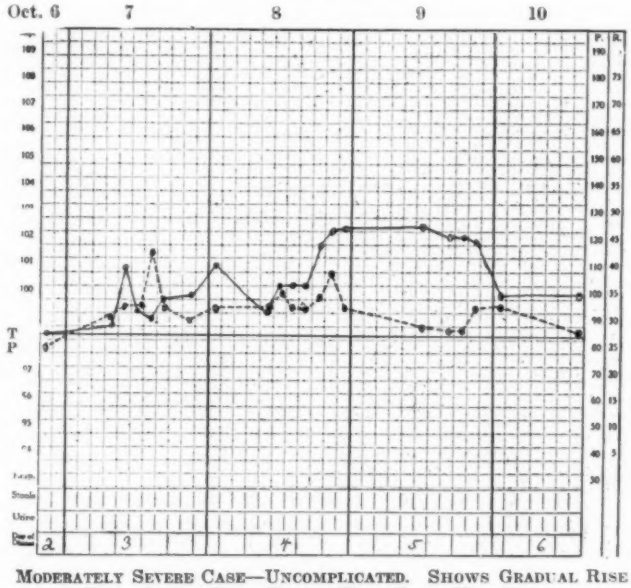
2. It is not primarily a local disease of the respiratory tract.

3. It presents a definite and characteristic clinical picture quite apart from the pulmonary complications.

4. The main features of the uncomplicated disease are a constant set of symptoms, characteristic erythema and appearance of the mouth, fever of determinate duration, and leucopenia.

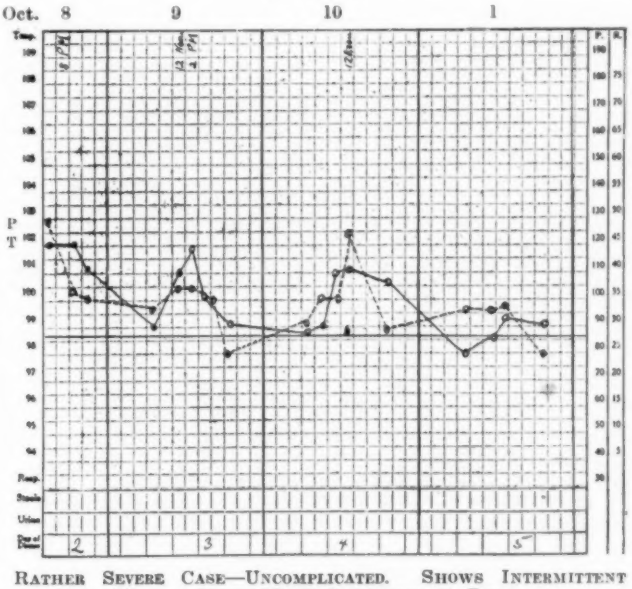
5. Proof is lacking that the Pfeiffer bacillus is the primary cause of uncomplicated influenza.

CHART II



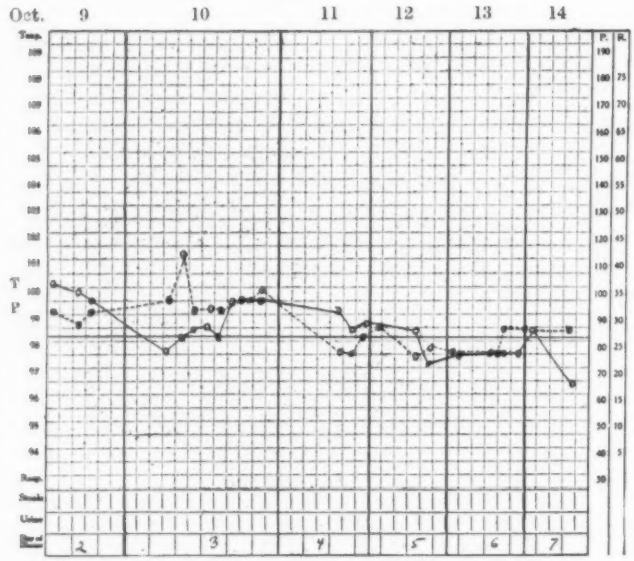

MODERATELY SEVERE CASE—UNCOMPLICATED. SHOWS GRADUAL RISE OF FEVER OVER 4 DAYS BEFORE HIGH POINT WAS REACHED.

CHART III



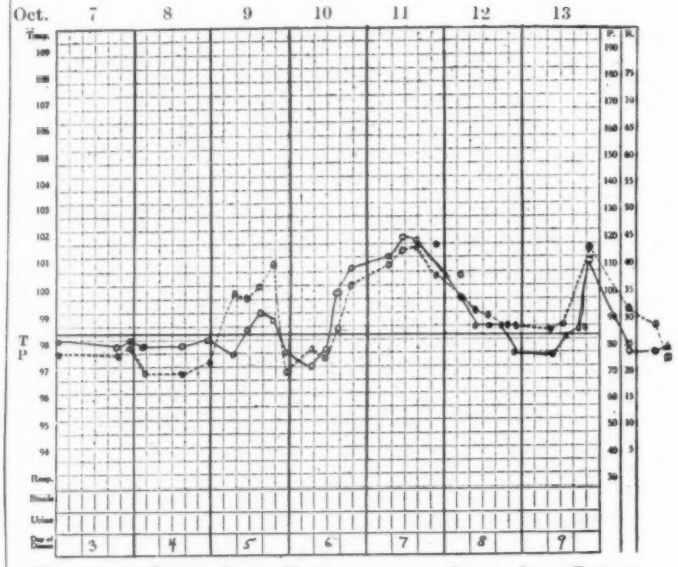

RATHER SEVERE CASE—UNCOMPLICATED. SHOWS INTERMITTENT TYPE OF FEVER WITH CORRESPONDING PULSE.

CHART IV



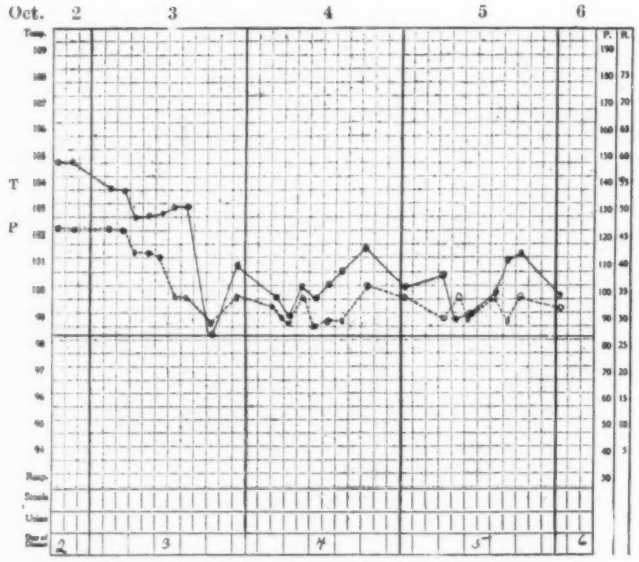

AN EXTREMELY SEVERE CASE. CHART SHOWING ONLY SLIGHT FEVER.

CHART V



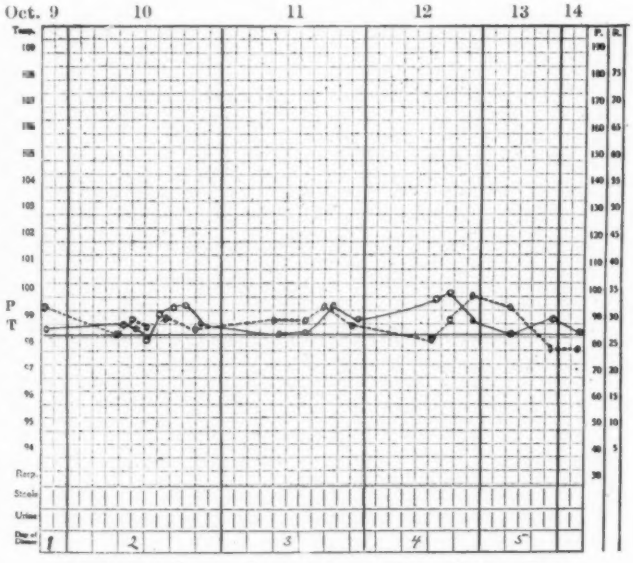

MODERATELY SEVERE CASE—UNCOMPLICATED. SHOWS LATE RISE OF TEMPERATURE ON THE 6TH TO 8TH DAY.

CHART VI



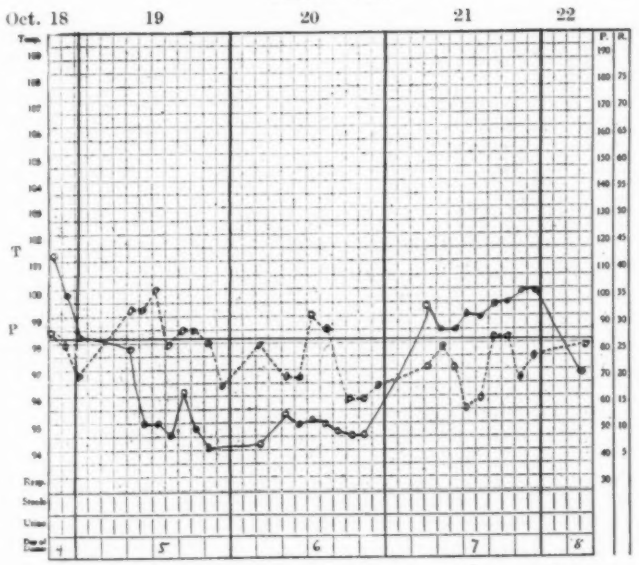

A FULMINATING CASE. CHART SHOWS VERY HIGH FEVER.

CHART VII



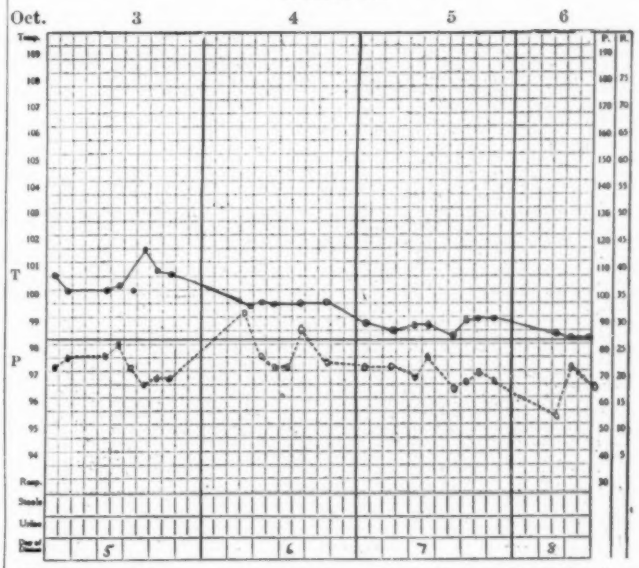

MODERATELY SEVERE CASE SHOWING VERY SLIGHT FEVER.

CHART VIII



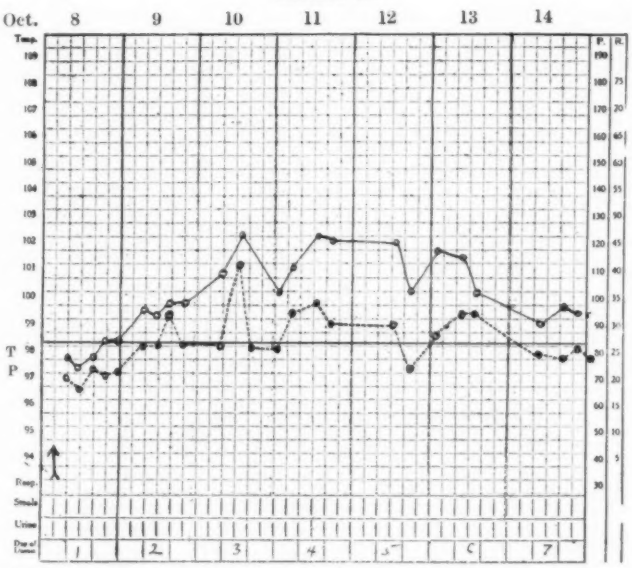

MODERATELY SEVERE CASE—UNCOMPLICATED. SHOWS FEVER FOLLOWED BY SUBNORMAL TEMPERATURE.

CHART IX



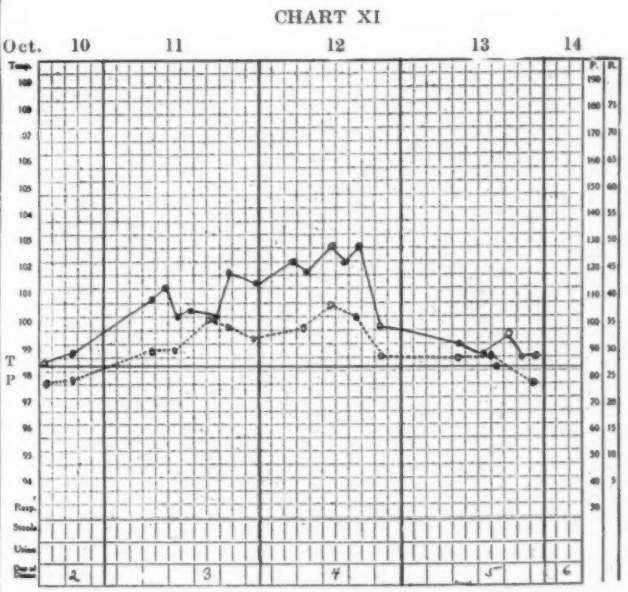

VERY SEVERE CASE—UNCOMPLICATED. SHOWS CHART FROM 5TH-8TH DAY. GRADUAL FALL OF TEMPERATURE—RELATIVE BRADYCARDIA—ABSOLUTE BRADYCARDIA IN CONVALESCENCE.

CHART X




A PATIENT WHO CONTRACTED INFLUENZA IN THE WARD. SYMPTOMS BEGAN AT ↑. SHOWS GRADUAL RISE OF TEMPERATURE.

CHART XI




A FULMINATING CASE WITH INTENSE SYMPTOMS ESPECIALLY HEADACHE. CHART SHOWS GRADUAL RISE OF FEVER. SUDDEN FALL OF FEVER WITH PROMPT RELIEF OF SYMPTOMS ON 5TH DAY—FOLLOWED BY PROSTRATION.

# THE BEHAVIOR OF THE BLOOD TOWARD OXYGEN IN INFLUENZAL INFECTIONS

By George A. Harrop, Jr.

*(From the Medical Clinic of The Johns Hopkins Hospital)*

The general clinical picture in the cases of bronchopneumonia occurring during the recent epidemic of influenza is too well known to need detailed restating. Outstanding features, which bear on the present discussion, are as follows: frequently an insidious onset towards the end of the acute influenza; cyanosis, often blended with the intense, dusky erythema of the uncomplicated influenza; absence during the early part of the attack of any marked respiratory distress; and, until the moment of collapse, good circulation. The pulse is often but little accelerated, and is nearly always of good quality. In most of the fatal cases, during a period of from 24 to 36 hours before death, the patient's condition is profoundly changed. The respirations are accelerated, the pulse becomes rapid and weak, and a most striking cyanosis rapidly develops. The patient may become unconscious, but frequently remains perfectly alert and apprehensive almost to the moment of death. The peculiar color of these patients suggested an examination of the oxygen content of the blood.

The oxygen content of the blood in lobar pneumonia has been studied by Peabody,[1] who found in most uncomplicated cases that the decrease of respiratory surface due to the consolidation is completely compensated for; that is, there is no demonstrable disturbance of the respiratory exchange, and the oxygen content of the blood is within normal limits. His estimations were made by the method of Barcroft and Haldane,[2] as modified by Brodie.[3] The oxygen content of the peripheral venous blood in his control cases varied between 9.23 and 15.02 volumes per cent. He found no definite relation between either temperature or respiration and the oxygen content of the blood. In a number of fatal cases of lobar pneumonia, where the termination was gradual, the patient becoming slowly weaker and more toxic, cyanosis increasing and pulmonary edema coming on, he found a progressive decrease in the oxygen content of the blood. In such instances, specimens taken at about the time of death showed a low oxygen-combining power. The fall in the latter was less marked than the fall in the actual oxygen content of the venous blood, although the two were roughly parallel. The lowest value for the oxygen-combining power at death he found to be 7.87 per cent. All of his other cases gave values above 13 per cent. He found similar phenomena in the blood of rabbits with a severe pneumococcic bacteriemia.[4] In experiments in which the pneumococcus was grown in a mixture containing unlaked red blood cells or hemoglobin, he showed, in collaboration with Butterfield, that methemoglobin is formed and may be demonstrated by spectroscopic methods. It is probably this alteration of the hemoglobin which lowers the power of the blood to take up oxygen.[5]

A fairly simple technique for estimating the oxygen content of the peripheral venous blood has been devised recently by Lundsgaard.[6] In determinations on 12 normal persons, he found that the oxygen content of the peripheral venous blood averaged about 13.50 volumes per cent, or about two-thirds that of the total oxygen capacity of the blood, which is variously stated. It is probably about 22 volumes per cent for the average normal individual.[7] He stresses the important point that the oxygen content of the venous blood is difficult to interpret, unless a simultaneous determination is made of the total oxygen-combining power of the hemoglobin. The difference between these two values he terms the *oxygen unsaturation* of the blood, since it is a measure of that part of the hemoglobin whose oxygen-combining power is not fully saturated. The oxygen unsaturation of the venous blood in his normal controls, as well as in cases with compensated circulatory disturbances with regular pulse, varied between 9 and 2.5 volumes per cent, the average being about 5.8 volumes per cent. There are very few clinical reports dealing with determinations of venous oxygen tension. Obvious difficulties have so far rendered estimations upon the arterial blood impracticable. They can be safely made, however,[8] and we shall report shortly our observations on the oxygen content of the arterial blood in a number of pulmonary and cardiac diseases.

The determinations included in this report have been made upon nine cases of post-influenzal bronchopneumonia, three of them fatal, and upon four uncomplicated cases of influenza, in the early hyperacute stage, when the characteristic dusky erythema or "cyanosis," was most striking. The oxygen content of the venous blood was determined by Lundsgaard's method. A pipette filmed with oxalate crystals was attached to a bit of rubber tubing and thence to the needle. After withdrawal, the blood was immediately transferred to a tube under a layer of oil, to prevent contact with the air. It was found that a glass syringe with a snugly-fitting greased plunger can be employed with equal facility,[9] the middle

[1] Peabody, F. W.: Jour. Exp. Med., 1913, XVIII, 7.

[2] Barcroft, J., and Haldane, J. S.: Jour. Physiol., 1902, XXVIII, 232.

[3] Brodie, T. G.: Jour. Physiol., 1909-10, XXXIX, 391.

[4] Peabody, F. W.: Jour. Exp. Med., 1913, XVIII, 1.

[5] Butterfield, E. E., and Peabody, F. W.: Jour. Exp. Med., 1913, XVII, 587.

[6] Lundsgaard, C.: Jour. Biol. Chem., 1918, XXXIII, 133.

[7] Palmer, W. W.: Jour. Biol. Chem., 1918, XXXIII, 119.

[8] Hürter: Deutsch. Arch. klin. Med., 1912, CVIII, 1.

[9] Means, J. H., and Newburgh, L. H.: Trans. Assn. Am. Phys., 1915, XXX, 58.

portion of the blood withdrawn being used for the oxygen content estimations and the remainder for determinations of the total oxygen capacity, which were done by the method of Van Slyke.[10] From the latter, the percentage of hemoglobin was calculated according to the commonly used standard of

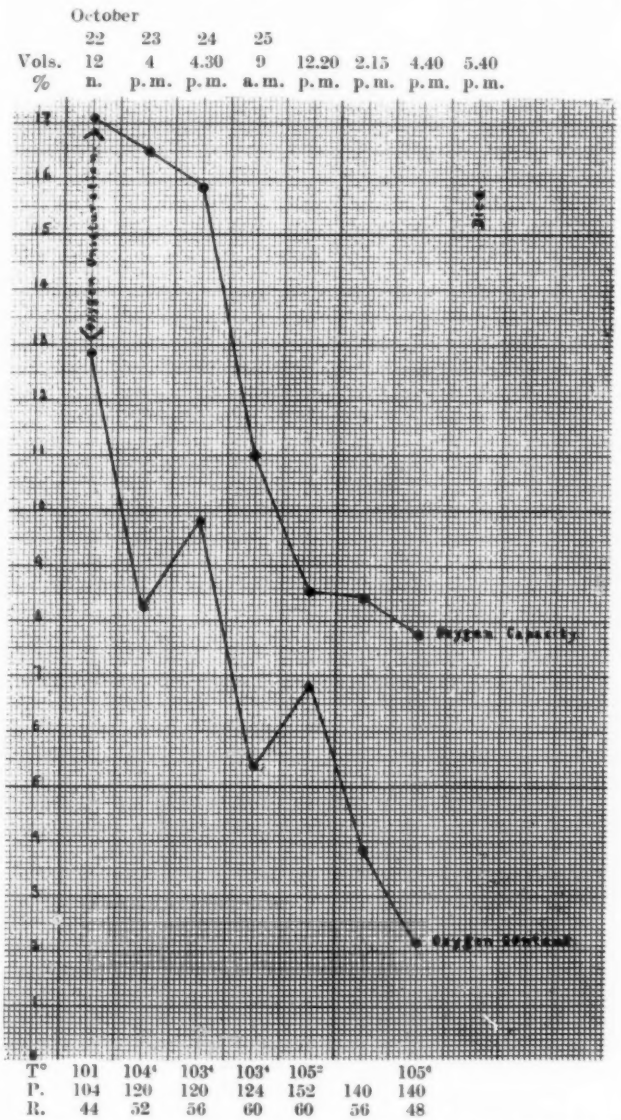



CHART 1.—The Oxygen Capacity and Content of the Peripheral Venous Blood of a Fatal Case of Bronchopneumonia. (Clinical Notes are Given in Table I, Case 7.)

Haldane,[11] using 18.5 volumes per cent of oxygen as equivalent to 100 per cent of hemoglobin. Two cubic centimeter samples were used and all determinations were made in duplicate within half an hour after collecting the sample. All of the collections were made from bed patients, and in only a few instances was it necessary to insert the needle more than once. Care was used to cause the least possible pain, so there was practically no change in the rate of pulse or respiration during the operation. The blood is withdrawn much more slowly than when a tourniquet is used. It is important to apply very little suction, or bubbles of air will be drawn in around the piston, rendering the specimen useless.

The determinations made upon specimens taken during the hyperacute febrile period from the cases of influenza with an extreme grade of erythema, are shown in Table 1.

No abnormality is seen either in the oxygen content or in the oxygen unsaturation.

The results from the cases of bronchopneumonia are shown in Table 2.

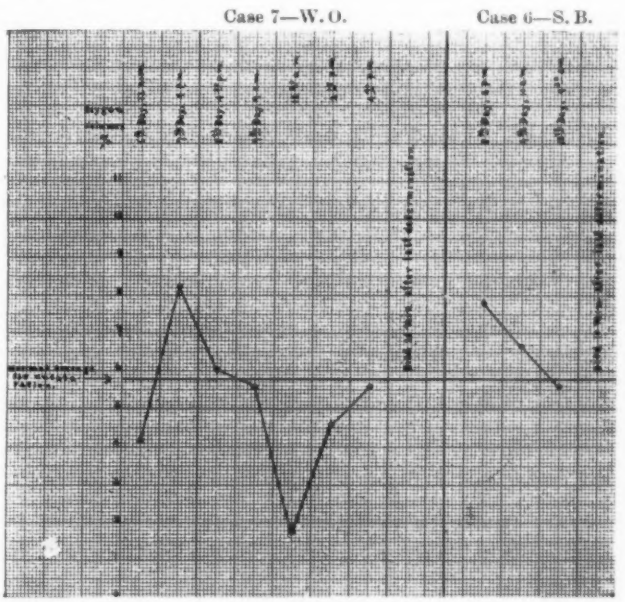



CHART 2.—Oxygen Unsaturation in Fatal Cases of Bronchopneumonia.

The six cases of post-influenzal bronchopneumonia (cases 1-6) which subsequently recovered, had definite physical evidence of consolidation during the course, with typical sputum, temperature curve and clinical phenomena. Four of them were exceedingly ill.

Three cases terminated fatally (cases 7-9). On one of these (case 9) there were but two determinations, the last nearly 24 hours before death. Both were within normal limits. On the other two cases, two or more determinations were made during the period of terminal collapse. In both there was a normal venous oxygen tension and capacity until the period of collapse occurred with its feeble, rapid pulse, rapid respirations and extreme cyanosis. Both the oxygen capacity and the oxygen content of the blood then fell rapidly and to a marked degree. The course of this case is shown on Chart 1.

[10] Van Slyke, D. D.: Jour. Biol. Chem., 1918, XXXIII, 127.
[11] Haldane, J., and Smith, J. L.: Jour. Physiol., 1900, XXV, 331.

TABLE 1.—HYPERACUTE CASES OF INFLUENZA WITH MARKED ERYTHEMA, PROSTRATION, AND FEVER. BLOOD CULTURES NEGATIVE

| Case | Name | Day of disease | Hour | Oxygen content venous blood | Total oxygen capacity | Oxygen unsaturation | Hemoglobin calculated from oxygen capacity (18.5 vol. % =100 %) | Temp. | Pulse | Resp. | Blood culture | Clinical data |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | H. | 4 | 10:45 a. m. | 14.35 | 18.97 | 4.62 | 102.0 | 100.2 | 92 | 24 | 0 | Fourth day. Marked erythema. Extreme prostration. |
| 2 | L. | 3 | 11:00 a. m. | 11.77 | 17.39 | 5.62 | 93.9 | 99. | 80 | 22 | 0 | Third day. Face flushed. Physical examination negative. |
| 3 | R. | 2 | 11:15 a. m. | 13.18 | 15.83 | 2.65 | 85.6 | 102. 8 | 100 | 20 | 0 | Second day. Rather marked prostration. Lungs clear. |
| 4 | M. | 2 | 10:30 a. m. | 12.01 | 18.70 | 6.69 | 100.1 | 102. | 98 | 20 | 0 | Second day. Marked flush of face, neck and thorax, with throat eruption. Prostration. Lungs negative. |

TABLE 2.—CASES OF BRONCHOPNEUMONIA FOLLOWING INFLUENZA

| Case | Name | Day of disease | Hour | Oxygen content venous blood | Total oxygen capacity | Oxygen unsaturation | Hemoglobin calculated from oxygen capacity (18.5 vol. % =100 %) | Temp. | Pulse | Resp. | Blood culture | Clinical data |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | S.B.F. | 7 | 9:40 a. m. | 15.33 | 18.68 | 3.35 | 101.0 | 101 | 90 | 26 | 0 | Frank consolidation of both lowers. Profuse green purulent sputum. Marked flush of cheeks and upper chest. Alert and restless. Cyanosis. |
| | | 12 | 11:35 a. m. | 7.39 | 16.04 | 8.65 | 86.7 | 99.1 | 96 | 24 | | Resolution taking place on right. Thick green sputum. Slight cyanosis. |
| | | 17 | 10:15 a. m. | 13.75 | 16.90 | 3.15 | 91.4 | 98.2 | 96 | 24 | | Left lower now resolving. Very pale. Looks worn out. |
| 2 | Mrs.F. | 8 | 10:40 a. m. | 14.08 | 16.60 | 2.52 | 89.7 | 103.4 | 112 | 24 | 0 | Cough with expectoration of small amount of blood-tinged sputum. Flush over cheeks and upper chest. Patch of consolidation at left lower. |
| 3 | D.O'B. | 16 | 12:20 p. m. | 7.46 | 14.20 | 6.74 | 76.8 | 99 | 100 | 24 | 0 | Striking bluish plum color of lips, face and neck. Consolidation of both lowers. |
| | | 23 | 10:30 a. m. | 5.68 | 11.27 | 5.59 | 60.9 | 98.6 | 100 | 22 | | Delayed resolution, both lowers. Peculiar color of face and neck persists. |
| 4 | E.W. | 14 | 5:20 p. m. | 10.52 | 16.60 | 6.08 | 89.7 | 104.8 | 100 | 32 | 0 | Consolidation of right lower and middle lobes. Bloody sputum. Apprehensive. |
| | | 17 | 10:30 a. m. | 10.19 | 13.65 | 3.46 | 73.8 | 98.3 | 80 | 26 | | First day following fall of temperature by crisis. Signs of resolution at right base. |
| 5 | M. A. | 15? | 10:30 a. m. | 11.05 | 18.60 | 7.55 | 100.6 | 101.4 | 135 | 38 | 0 | Empyema following pneumonia, with probably some consolidation remaining at right base. Flushed. Moderate cyanosis. |
| | | 18? | 10:00 a. m. | 15.25 | 18.55 | 3.30 | 100.2 | 99.8 | 100 | 34 | | Following operation. Rather marked cyanosis. |
| 6 | H. S. | 4 | 12:30 p. m. | 9.43 | 18.15 | 8.72 | 98.6 | 103.6 | 100 | 24 | 0 | Bloody sputum. Consolidation of left lower. Well marked cyanosis. Apprehensive. |
| | | 6 | 10:45 p. m. | 9.71 | 18.10 | 8.39 | 96.2 | 99 | 88 | 20 | | Condition slightly improved. Still marked cyanosis. Less sputum. No difficulty in breathing. |
| 7 | W.O | 6 | 12:00 n. | 12.88 | 17.10 | 4.22 | 92.4 | 101.9 | 104 | 44 | 0 | Frank consolidation of both lowers. Jaundice. Difficult to rouse. Rapid, shallow respiration. No particular cyanosis. |
| | | 7 | 4:00 p. m. | 8.25 | 16.50 | 8.25 | 89.2 | 104.4 | 120 | 52 | | No spread of consolidation. Somewhat brighter. Less jaundice. |
| | | 8 | 4:30 p. m. | 9.80 | 15.85 | 6.05 | 85.7 | 103.4 | 120 | 56 | | Jaundice much less. Rarely coughs. No sputum. No spread of consolidation. Practically in coma. |
| | | 9 | 9:00 a. m. | 5.38 | 11.00 | 5.62 | 59.5 | 103.4 | 124 | 60 | Pneumococcus IV. | Evident collapse with well-marked, livid cyanosis. Cannot be roused. Many râles at both bases. |
| | | 9 | 12:20 p. m. | 5.80 | 7.53 | 1.73 | 40.7 | 105.2 | 152 | 60 | | |
| | | 9 | 2:15 p. m. | 3.84 | 8.44 | 4.60 | 45.6 | ..... | 140 | 56 | | |
| | | 9 | 4:40 p. m. | 2.17 | 7.74 | 5.57 | 41.8 | 105.6 | 140 | 48 | | Patient died about ten minutes after this determination. |
| 8 | S. B. | 8 | 2:00 p. m. | 9.26 | 17.10 | 7.84 | 92.4 | 99.2 | 128 | 48 | Pneumococcus, not grouped | Orthopnea. Cheeks flushed. Incomplete consolidation of both lowers, with many moist râles, especially on the left. |
| | | 9 | 10:00 a. m. | 8.65 | 15.34 | 6.69 | 82.9 | 96.0 | 124 | 44 | | Subnormal temperature. Sweating. Cyanosis. Frank consolidation of both lowers. Complete. |
| | | 10 | 9:30 a. m. | 2.65 | 8.24 | 5.59 | 44.5 | 95.6 | 120 | 36 | | Weak, collapsed, extreme cyanosis. Died 20 minutes later. |
| 9 | H. H. | 4 | 10:10 p. m. | 10.45 | 12.90 | 2.45 | 69.7 | 104.4 | 140 | 68 | Pneumococcus, not grouped | Moderate cyanosis. Consolidation at right and left lowers, especially right. |
| | | 5 | 11:20 a. m. | 8.07 | 11:98 | 3.91 | 64.8 | 105.5 | 180 | 72 | | Consolidation spreading. Died 24 hours later. |

It is impossible in these two cases to explain the very great diminution in the oxygen-combining power and in the oxygen content of the blood just before death. Possibly the conversion of hemoglobin into methemoglobin progressed to a marked degree during the prolonged period of terminal collapse. If this be true, it would indicate that this conversion can proceed gradually to a marked degree without necessarily causing death, the circulatory mechanism to a certain point compensating for the lack of oxygen-carrying material, possibly by an increased velocity of the blood flow. On the other hand, it is possible that some other factor still unknown may play a part in altering the oxygen-carrying power of the blood.

The behavior of the curve for oxygen unsaturation is entirely unexpected. There is practically no deviation from the normal range of values up to the time of death.

In the five uncompensated cardiac cases studied by Lundsgaard [12] he found values for the oxygen unsaturation which were constantly higher than the normal values, ranging instead between 9.7 and 15.2 volumes per cent. He considered cyanosis one of the factors which have a very close relation to the amount of oxygen unsaturation in cardiac decompensation. There seems, therefore, to be an essential difference between the effect upon the circulatory system which causes the cyanosis in cardiac disease and that which produced the cyanosis in these cases of bronchopneumonia.

[12] Lundsgaard, C.: Jour. Exp. Med., 1918, XXVII, 179.

### CONCLUSION

1. The oxygen capacity and oxygen content of blood withdrawn from a peripheral arm vein have been determined in four cases of influenza during the hyperacute stage and in nine cases of bronchopneumonia following influenza.

2. Both oxygen content and oxygen unsaturation showed normal values in uncomplicated influenza cases.

3. In none of the cases of bronchopneumonia which recovered, and not until the terminal collapse in the fatal cases, has the venous oxygen content or the amount of oxygen unsaturation been abnormal. The values seem independent of temperature, pulse, respiration and extent of lung involvement.

4. In two fatal cases with septicemia, after the terminal collapse, there was a progressive fall in both the oxygen-combining power and the oxygen content of the venous blood, in general, parallel.

5. There was no increase at any stage of the disease in the values for the oxygen unsaturation of the blood.

# BACTERIOLOGICAL FINDINGS IN EPIDEMIC INFLUENZA

By S. E. HOWARD, M. D.

*(From the Medical Clinic of The Johns Hopkins Hospital)*

The cultures reported in this paper were taken in the cases reported in the foregoing paper by Dr. Bloomfield and Dr. Harrop. At the onset of the epidemic an attempt was made to take cultures from the nasopharynx and the blood in every case of epidemic influenza admitted to The Johns Hopkins Hospital, and also to make cultures from the sputum whenever any was present. With the sudden increase in the number of cases it was impossible to carry out this plan. A special study was then made of patients who had a very sudden, severe onset, and who were admitted to the hospital wards immediately; cultures from the nasopharynx and the blood were taken from these patients as soon after admission as possible. Cultures from the nasopharynx were repeated in many of them during convalescence. From all patients who had any sputum an attempt was made to get a fresh specimen for culture. In all cases of pneumonia, which were considered critically ill, blood cultures were made; in most of these cases the cultures were repeated daily until marked improvement or death occurred.

The cultures from the nasopharynx were made on blood-agar plates. The agar contained about 5 per cent blood, and was poured into petri dishes with a diameter of 5½ inches. To obtain the culture, a sterile swab was used, consisting of a piece of very stiff wire, the tip of which was wound with absorbent cotton, and bent at an angle of 80°. With the tongue depressed, it was possible to slip the cotton-covered tip behind the uvula, thoroughly rub it over the nasopharynx, and extract it through the mouth, without coming in contact with the tongue or any parts of the buccal mucous membrane. This method of obtaining the culture seemed more satisfactory than using a West tube or inserting a swab through the nostrils. As soon as the swab was withdrawn, one side of a blood agar plate was streaked with it. A second sterile swab was rubbed first over the streak and then over the rest of the plate; by this method individual colonies of the bacteria present were obtained. The results of the cultures obtained from the nasopharynx by this technique are given in Table I.

The sputum for culture was obtained as follows: First, the patient was asked to clear his throat and to rinse his mouth thoroughly with Dobell's solution. Then he was asked to cough hard and to try to raise sputum from the lungs. Only sputum obtained after a good paroxysm of coughing was used. This was received in a sterile petri dish, carried immediately to the laboratory, and cultured as soon as possible, being kept on ice if any delay was necessary. Most of the specimens were thin, mucoid, often blood-tinged and difficult to wash. Whenever possible, the specimens were washed in six dishes of sterile salt solution; the more friable ones could only be washed three or four times. It was a striking fact

TABLE I.—NASOPHARYNX CULTURES—SUMMARY

| Type of case | Results | | | | |
|---|---|---|---|---|---|
| | Predominating organisms | | | | Organisms present in small numbers |
| | Pneumococci | Green streptococci | *B. influenzæ* | Other organisms | |
| Cultures on admission from cases with hyperacute onset. (18 cases.) | 2 cases. Both Group IV. | 8 cases. | No cases. | 4 cases had green colonies which may have been pneumococci or streptococci. Not identified. In 4 cases staph. albus predominated. | In 2 cases small gram-negative bacilli, *morphologically like B. influenzæ*, were seen in smears from cultures, but were not isolated in pure culture. Staph. albus, green streptococci and pneumococci also occurred in cultures in which they did not predominate. |
| Cultures from 12 of the above cases were taken during convalescence, about one week after admission. No pneumonias in this group. | The results of these cultures were practically identical with those of the cultures taken on admission, except that *more influenza bacilli were found*, though they were *never* present as the predominating organism. From two of these cases *B. influenzæ* was isolated in pure culture. In three others, small gram-negative bacilli, morphologically resembling *B. influenzæ*, were seen in smears from the original culture, but not isolated in pure culture. | | | | |
| | Predominating organisms | | | | Organisms present in small numbers |
| | Pneumococci | Green streptococci | *B. influenzæ* | Other organisms | |
| Cultures from 9 convalescents not previously cultured. | 1 case. Group IV. | 4 cases. | None. | Staphylococcus in 2 cases. Green colonies of pneumo. or strepto. not identified in 2 cases. | 2 cases showed small gram-negative bacilli, morphologically resembling *B. influenzæ*. Not isolated in pure culture. |
| Cultures from 10 patients who did not have influenza. | 3 cases of Group IV. 1 case of atypical Group II. | 1 case. | 1 case. | Staphylococcus in 2 cases. Unidentified pneumo. or strepto. in 1 case. | In 1 case small gram-negative bacilli, morphologically resembling *B. influenzæ* were seen in smears from cultures, but not isolated in pure culture. |

73 other nasopharynx cultures were taken at the onset of the epidemic, including all the first cases of epidemic influenza in the hospital. In only one of these did *B. influenzæ* predominate; in two others small gram-negative bacilli morphologically resembling it were seen, but not isolated in pure culture.

that the sputum we obtained in most of the cases was not the type of sputum which Pfeiffer[1] describes as typical of the cases in which he found *B. influenzæ*. In the few instances in which we found *B. influenzæ* as the predominating organism, the sputum was of a type different from that found in the majority of our cases; it was yellow-green in color, definitely purulent, tenacious and readily washed. These cultures were made on blood agar in petri dishes. The results of the sputum cultures are given in Table II.

Green streptococci, pneumococci and staphylococci also occurred in cultures in which they did not predominate.

In differentiating pneumococci (Type IV) from green streptococci, bile solubility was adopted as the criterion. Some partiality soluble strains were found. Most of the strains classified as "green streptococci" formed long chains in meat infusion broth and produced relatively slight turbidity, but an abundant sediment. Most of the bile soluble strains caused diffuse turbidity with a variable amount of sediment. Morphologically, the majority of the insoluble forms were more or less lance-shaped; many of them were markedly elongated, so as to be almost bacillary in type; more so than the typical pneumococcus. On blood agar plates, individual colonies tended to be smaller and less moist than typical pneumococcus colonies; and on blood-agar slants

TABLE II.—SPUTUM CULTURES—SUMMARY
(Cultures were done in 36 cases)

| Predominating organisms | | | |
|---|---|---|---|
| Pneumococci | Green streptococci | *B. influenzæ* | Other organisms |
| Group IV. 4 cases. | 18 cases. | 3 cases. | 6 cases—green colonies, which may have been either pneumococci or green streptococci; the organisms were not identified. |
| Group III. 1 case. Patient had Group III pneumonia previous to present illness. | ..... | ..... | 1 case—a pure culture of staphylococcus aureus was present. |
| Groups I & II. None. | ..... | ..... | In the remaining cases, mic. catarrhalis or staph. albus predominated. |

ORGANISMS PRESENT BUT NOT PREDOMINATING

*In 13 cultures* in which *B. influenzæ* did not predominate small gram-negative bacilli, which *morphologically* were *like B. influenzæ*, were seen in smears from the original culture or in fresh sputum. In these cases we were unable to isolate this organism in pure culture, as very few of these bacilli were present.

[1] Pfeiffer, R., and Beck, M.: Weitere Mittheilungen über den Erreger der Influenza. Deutsch. med. Wchnschr., 1892, XX, 465.

there was a greater tendency to diffuse greenish discoloration of the agar. All of the green streptococci tested were readily phagocytable in normal serum. Those isolated from the nasopharynx of control cases seemed identical with strains obtained from influenza patients.

In making cultures from the blood, the usual technique was employed. In addition to pouring blood-agar plates and adding the blood to glucose broth and litmus milk, in many cases blood was added to ascitic-meat-infusion broth. The results of the blood cultures are given in Table III.

TABLE III.—BLOOD CULTURES—SUMMARY

| Type of case | Result |
|---|---|
| Uncomplicated cases at onset.—Cases with particularly acute onset. Cultures made in 18 cases on day of admission. | No growth in any culture. |
| Patients with pneumonia who recovered.—Cultures taken when patients were in critical condition. 28 cultures from 12 patients. | No growth in any culture. |
| Patients with pneumonia who died.—Cultures taken within 24 hours of death in all but 2 cases. 27 cultures in 13 cases. | 3 cases.—Pneumococcus Group IV, 23+%.<br>1 case.—Pneumococcus Group III, 7+%.<br>1 case.—Pneumococcus (Group not determined), 7+%.<br>1 case.—Hemalytic streptococcus, 7+%.<br>7 cases.—No growth, 55+%. |

In conclusion, we feel that none of the organisms isolated may be regarded as the cause of epidemic influenza. Our own results, compared with the summary of European literature on this subject[2] and the more recent work of Nuzum, *et al.*,[3] Strouse and Bloch,[4] etc., convince us that the *B. influenzæ* of Pfeiffer is merely a secondary invader, though in some localities, as in the cases reported by Keegan,[5] it may be a frequent cause of terminal bronchopneumonia. The other organisms isolated may also be regarded either as normal inhabitants of the mouth or as secondary invaders. The primary cause of epidemic influenza, we believe, is still unknown.

I am indebted to Dr. Charles W. Young for the isolation and identification of organisms from many of these cultures.

[2] Abstracts of Foreign Literature Compiled by British Medical Research Committee. Jour. Am. Med. Assn., 1918, LXXI, 1573.

[3] Nuzum, J. W.; Pilot, I.; Stangl, F. H.; Bonar, B. E.: Pandemic Influenza and Pneumonia in a Large Civil Hospital. Jour. Am. Med. Assn., 1918, LXXI, 1562.

[4] Strouse, S., and Bloch, L.: Notes on the Present Epidemic of Respiratory Disease. Jour. Am. Med. Assn., 1918, LXXI, 1568.

[5] Keegan, J. J.: The Prevailing Pandemic of Influenza. Jour. Am. Med. Assn., 1918, LXXI, 1051.

# ECTOPIC PREGNANCY

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## INCIDENCE

In the 27 years from 1890 to 1916 inclusive, there have been 303 patients with ectopic pregnancy in the Gynecological Service of The Johns Hopkins Hospital who were operated upon. There have been 22,688 patients admitted to the Gynecological Service during the 27 years, of which 303 had extrauterine pregnancies, an incidence of 1.3%.

TABLE SHOWING THE NUMBER OF PATIENTS WITH EXTRAUTERINE PREGNANCIES EACH YEAR

| Year | Number of patients | Year | Number of patients | Year | Number of patients | Year | Number of patients | Year | Number of patients |
|---|---|---|---|---|---|---|---|---|---|
| 1890 | 2 | 1896 | 6 | 1902 | 8 | 1908 | 23 | 1914 | 14 |
| 1891 | 3 | 1897 | 1 | 1903 | 15 | 1909 | 23 | 1915 | 13 |
| 1892 | 4 | 1898 | 8 | 1904 | 23 | 1910 | 13 | 1916 | 13 |
| 1893 | 8 | 1899 | 7 | 1905 | 23 | 1911 | 15 | | |
| 1894 | 7 | 1900 | 10 | 1906 | 13 | 1912 | 11 | | |
| 1895 | 3 | 1901 | 10 | 1907 | 16 | 1913 | 11 | Total | 303 |

*Race.*—Negroes, 101; white, 202. Total, 303.

Of these 22,688 patients, 17,412 were white and 5276 were negroes. There were 202 cases of extrauterine pregnancy among the whites (1.16%) and 101 among the negroes (1.91%).

## AGE

Of this series of cases the age was recorded 300 times. The youngest patient was a 15-year-old white girl, married seven months previously to admission and never pregnant before. An unruptured left tubal pregnancy was removed at operation. The oldest patient was a 45-year-old negress, who had given birth to three full-term children. At operation a full-term lithopedion, which had been in the abdomen for four years was removed (Reported by J. G. Clark, The Johns Hopkins Hospital Bulletin, 1897, VIII, and in Kelly's Operative Gynecology, Vol. II). Of this series 182 (61%) occurred in the decade 24 to 33 years inclusive. Seven patients were under 20 years and ten were over 40 years of age.

TABLE SHOWING AGES OF 300 PATIENTS

| Age | Number of patients | Age | Number of patients | Age | Number of patients | Age | Number of patients | Age | Number of patients |
|---|---|---|---|---|---|---|---|---|---|
| *yrs.* | | *yrs.* | | *yrs.* | | *yrs.* | | *yrs.* | |
| 15 | 1 | 22 | 10 | 28 | 25 | 34 | 11 | 40 | 4 |
| 17 | 1 | 23 | 11 | 29 | 17 | 35 | 13 | 41 | 2 |
| 18 | 3 | 24 | 22 | 30 | 18 | 36 | 9 | 42 | 4 |
| 19 | 2 | 25 | 18 | 31 | 17 | 37 | 6 | 43 | 2 |
| 20 | 6 | 26 | 12 | 32 | 13 | 38 | 8 | 44 | 1 |
| 21 | 12 | 27 | 20 | 33 | 20 | 39 | 11 | 45 | 1 |

### MARITAL HISTORY

In a series of 284 there were 14 unmarried, two widows and nine twice married.

TABLE SHOWING TIME OF ADMISSION AFTER MARRIAGE

| Time married | Number of patients | Time married | Number of patients | Time married | Number of patients | Time married | Number of patients |
|---|---|---|---|---|---|---|---|
| | | *yrs.* | | *yrs.* | | *yrs.* | |
| 2 wks... | 1 | 1 | 9 | 9 | 8 | 18 | 9 |
| 4 wks... | 1 | 2 | 22 | 10 | 14 | 19 | 3 |
| 6 wks... | 1 | 3 | 18 | 11 | 9 | 20 | 7 |
| 2 mos... | 1 | 4 | 13 | 12 | 17 | 21 | 6 |
| 4 mos... | 1 | 5 | 15 | 13 | 11 | 22 | 2 |
| 5 mos... | 1 | 6 | 12 | 14 | 8 | 23 | 3 |
| 7 mos... | 1 | 7 | 21 | 15 | 9 | 26 | 1 |
| 8 mos... | 1 | 8 | 18 | 16 | 6 | 27 | 1 |
| | | | | 17 | 8 | Total | 268 |

### PREVIOUS PREGNANCIES

In the histories of 275 patients, the number of pregnancies prior to the ectopic pregnancy was recorded. In 57 (21%) there had been no previous pregnancy and of the 218 (79%) who had been pregnant before, 207 (95%), 75% of the whole series, had given birth to full-term babies and 11 (5%), 4% of the whole series, had had only miscarriages. Instrumental deliveries had been performed on 19 patients (9% of those who had had full-term pregnancies). Histories of prolonged puerperia associated with chills, fever and abdominal pain were obtained from 38 patients (17.5% of all patients previously pregnant).

TABLE SHOWING NUMBER OF PREVIOUS PREGNANCIES

| Number of miscarriages | Number of patients | Number of children | Number of patients | Total pregnancies | Number of patients |
|---|---|---|---|---|---|
| 1 | 65 | 1 | 77 | 0 | 57 |
| 2 | 25 | 2 | 32 | 1 | 67 |
| 3 | 8 | 3 | 27 | 2 | 42 |
| 4 | 5 | 4 | 21 | 3 | 22 |
| 5 | 2 | 5 | 17 | 4 | 22 |
| 6 | 2 | 6 | 14 | 5 | 16 |
| Total | 107 | 7 | 8 | 6 | 16 |
| | | 8 | 2 | 7 | 13 |
| | | 9 | 2 | 8 | 8 |
| | | 10 | 3 | 9 | 2 |
| | | 11 | 1 | 10 | 3 |
| | | 12 | 0 | 11 | 1 |
| | | 13 | 1 | 12 | 1 |
| | | 14 | 2 | 13 | 1 |
| | | Total | 207 | 14 | 1 |
| | | | | 15 | 2 |
| | | | | 16 | 1 |
| | | | | Total | 275 |

The interval between the last pregnancy and admission to the hospital for an ectopic pregnancy was noted in the histories of 226 patients, the shortest interval being three months and the longest 19 years. The interval was between one and seven years in 168 patients (74%).

TABLE SHOWING THE INTERVAL BETWEEN THE LAST PREGNANCY AND ADMISSION TO THE HOSPITAL FOR ECTOPIC PREGNANCY

| Time | Number of patients | Time | Number of patients | Time | Number of patients | Time | Number of patients | Time | Number of patients |
|---|---|---|---|---|---|---|---|---|---|
| *mos.* | | *mos.* | | *yrs.* | | *yrs.* | | *yrs.* | |
| 3 | 1 | 9 | 5 | 3 | 23 | 9 | 5 | 15 | 3 |
| 4 | 1 | 10 | 1 | 4 | 22 | 10 | 8 | 16 | 1 |
| 5 | 4 | 11 | 2 | 5 | 13 | 11 | 4 | 17 | 1 |
| 6 | 4 | 12 | 20 | 6 | 20 | 12 | 6 | 18 | 1 |
| 7 | 1 | 18 | 15 | 7 | 19 | 13 | 1 | 19 | 2 |
| 8 | 1 | 2 | 36 | 8 | 5 | 14 | 1 | Total | 226 |

### PREVIOUS OPERATIONS

Forty-five patients had had operations prior to admission for ectopic pregnancy.

*Dilatation* and *curettage* had been performed on 15 patients for bleeding caused by the ectopic pregnancy; two of these operations were done in this hospital. One patient was curetted twice before admission for bleeding caused by the ectopic pregnancy.

Curettage was performed on 12 patients, from one to five years before their admission and simple dilatation of the cervix twice for sterility.

*Incision of Bartholin gland abscess,* five years before; one patient.

*Pelvic puncture* for inflammatory disease; three patients.

*Exploratory laparotomy* five years before; one patient.

*Multiple myomectomy* five years before; one patient.

*Ovarian tumor* removed; one patient.

*Tumor* removed and *appendectomy;* six years before; one patient.

*Parovariancystectomy,* right; *suspension of uterus; appendectomy;* two years before (Gyn. No. 16,409).

*Suspension of uterus* and *appendectomy;* 18 months before (Gyn. No. 15,751).

*Salpingo-oöphorectomy,* left, and *appendectomy;* one and two years ago, for chronic pelvic inflammatory disease; two patients.

*Salpingo-oöphorectomy,* right, and *appendectomy;* one patient.

*Appendectomy* (only); three patients.

*Appendectomy* and *nephropexy* were done in another city on one patient for the symptoms caused by a right tubal pregnancy about six and eight weeks prior to admission to this hospital.

Five patients have been operated upon twice in this hospital for ectopic pregnancy.

*Pelvic puncture,* once.

*Salpingectomy* (alone), twice.

*Salpingo-oöphorectomy,* twice.

### COMPLAINT

The symptoms that patients complained of on admission were as follows:

| | |
|---|---|
| Bleeding | 93 |
| Pain, general abdominal or not specified | 99 |
| Pain in lower abdomen | 69 |
| Pain in right lower quadrant of abdomen | 33 |
| Pain in left lower quadrant of abdomen | 33 |
| Pain in back | 20 |
| Pain designated as "bearing-down," 4 times; and as "cramp-like," 4 times. | |
| Tumor in abdomen | 17 |
| Tumor in right lower quadrant of abdomen | 1 |
| Tumor in left lower quadrant of abdomen | 4 |
| Swelling of abdomen | 3 |
| Tenderness of abdomen | 4 |

| | |
|---|---|
| Pregnancy | 2 |
| Miscarriage | 1 |
| Amenorrhœa | 1 |
| Dysmenorrhœa | 2 |
| Vomiting | 9 |
| Nausea | 6 |
| Diarrhœa | 1 |
| Pain on defecation | 1 |
| Dysuria | 2 |
| Pollakiuria | 1 |
| Fainting | 1 |

From the foregoing list we see that the most common causes for which these patients seek medical attention are pain, complained of by 254 (84%) bleeding, complained of by 93 (31%) and tumor, complained of by 22 patients (7%).

### SYMPTOMS

| | | |
|---|---|---|
| Onset (1) Acute without prodromal symptoms other than bleeding or a missed period | 146 | (48%) |
| (2) Acute with prodromal symptoms | 72 | (24%) |
| (3) Gradual without acute attacks | 84 | (28%) |
| Irregular bleeding | 229 | (76%) |
| Nausea | 146 | (48%) |
| Vomiting | 126 | (42%) |
| Tumor | 45 | (15%) |
| Fainting | 38 | (13%) |
| Fever | 29 | (10%) |
| Chills | 12 | (4%) |
| Weakness | 87 | (29%) |
| Defecation painful | 28 | (9%) |
| Urinary frequency | 40 | (13%) |
| Burning on voiding | 27 | (9%) |
| Pain on voiding | 87 | (29%) |
| Loss of weight | 6 | (2%) |
| Bad taste in mouth | 3 | (1%) |
| Patients believing themselves to be pregnant | 11 | |
| Patients not suspecting pregnancy | 3 | |
| Patients suspecting an abortion | 1 | |
| Patients who had felt life | 1 | |
| Patients having a sensation of fluid in the abdomen | 1 | |
| Patients who had passed complete casts of the uterus | 2 | |
| Patients complaining of pain in the abdomen not otherwise qualified | 131 | (43%) |
| Pain, general abdominal | 21 | (7%) |
| Pain, limited to the lower abdomen | 28 | (9%) |
| Pain, limited to the lower left quadrant | 43 | (14%) |
| Pain, limited to the lower right quadrant | 41 | (13%) |
| Abdominal pain over pelvis, with pain in the epigastrium | 2 | |
| Abdominal pain over pelvis, with pain in the umbilical region | 1 | |
| Abdominal pain over pelvis, with pain in the bladder | 1 | |
| Abdominal pain over pelvis, with pain in the rectum | 2 | |
| Abdominal pain over pelvis, with pain in the flanks | 2 | |
| Abdominal pain over pelvis, with pain in the thighs | 1 | |
| Abdominal pain over pelvis, with pain in the legs | 2 | |
| Abdominal pain over pelvis, with pain in the right shoulder | 2 | |
| Abdominal pain over pelvis, with pain in the chest | 1 | |
| Patients complaining of backache | 19 | |
| Patients complaining of headache | 2 | |

*Pain.*—The symptoms that a patient considers as sufficiently unusual to cause her to seek medical attention are produced in the vast majority of cases by intraperitoneal bleeding. A history of abdominal pain was procured from 300 patients (99%), the other three patients stated positively that there had been no abdominal pain or discomfort and they came to the clinic on account of irregular bleeding. In each of these three patients an unruptured tubal pregnancy was found at operation, but no evidence of any clot or free blood in the peritoneal cavity.

The onset of the symptoms may be acute without other prodromal symptoms, although there is usually a history of a missed period or of irregular bleeding. In a second type there is an acute attack following prodromal symptoms, which the patient sometimes ascribes to her pregnancy. A third type of patient gives a history of gradual onset without an acute attack.

Recurring attacks of pain occurred in 102 cases (34%); seventeen patients complained especially of soreness and tenderness, rather than of definite pains. In several instances the pain was of several years' duration, generally with a recent exacerbation, but in each instance at operation some other condition, usually chronic pelvic inflammatory disease, was also present.

The pains seem rarely to radiate. The character of the pain was described as violent, agonizing or severe in 90 cases, cramping in 41, colicky in four, bearing down in 14, labor-like in nine, shooting, cutting or sticking in six and as dull or aching in 29.

Pain or irritation in the rectum and bladder occur after intraperitoneal hemorrhage, most often when clots have collected in the pelvis and adhesions have formed. Pain and vaginal bleeding often occur about the same time. Myssey (St. Paul Med. Jour., 1914, XVI, 588) states that pain on defecation is almost pathognomonic of the condition, but in our experience, this symptom is also frequently present in cases of pelvic inflammatory disease.

### MENSTRUAL HISTORY

One hundred and three patients (34%) stated definitely that they had missed one or more periods; and 31 (10%) said that their last period had been overdue for from one to five weeks, while 52 (17%) had noticed that the last period was abnormal in some other respect.

| Number of periods missed | Number of patients | Number of periods missed | Number of patients |
|---|---|---|---|
| 1 | 42 | 7 | 1 |
| 2 | 34 | 8 | 2 |
| 3 | 14 | 9 | 0 |
| 4 | 2 | 10 | 3 |
| 5 | 4 | 11 | 1 |
| 6 | 0 | Total | 103 patients. |

| | |
|---|---|
| Increased frequency of menstruation | 14 |
| Constant bleeding since last period | 60 |
| No irregular bleeding | 49 |
| No irregular bleeding and no periods missed | 18 |
| Periods normally regular | 219 |
| Periods normally irregular | 30 |

| | |
|---|---|
| Last menstrual period: | |
| Overdue 1 week | 11 |
| Overdue 2 weeks | 16 |
| Overdue 3 weeks | 2 |
| Overdue 4 weeks | 1 |
| Overdue 5 weeks | 1 |
| Ahead of regular time | 12 |
| Shorter than usual | 5 |
| Longer than usual | 20 |
| Flow decreased | 13 |
| Flow increased | 9 |
| Color abnormal | 5 |

Nausea and vomiting occurred in a few cases, as in normally pregnant women and the patients with these symptoms considered themselves pregnant. In the great majority, however, there was a history pointing to intraperitoneal hemorrhage before nausea or vomiting had occurred.

Abdominal masses were noticed by the patients in cases of advanced pregnancy and where a walled-off hematocele was present.

Fainting occurred in some cases where there was profuse intraperitoneal hemorrhage.

Chills and fever were unusual symptoms and always suggested the gravest complications.

Weakness is generally present in the more anæmic.

Loss of weight was noticed only in advanced tubal pregnancy, as also was the complaint of a bad taste in the mouth.

The notes in our histories as to whether the patient considered herself pregnant are very incomplete, and no conclusions can be drawn from them except that not all believed that they were pregnant.

## SIGNS

In the following tabulation of physical signs, it is notable that many of the presumptive signs of intrauterine pregnancy are not present in the majority of this series of ectopic pregnancies. In the larger percentage of the cases in which the table gives "a softened and enlarged cervix or fundus" the notes were "slightly softened" or "slightly enlarged" and often there was a difference of opinion in those cases examined by two men. We believe that most cases of tubal pregnancy show no very definite gross changes in the cervix and uterine body, unless the fœtus is living. In no case was a positive Hegar's sign recorded. Vaginal cyanosis was not marked in any case.

The usual absence of definite muscle spasm or rigidity is in accordance with the signs of most pelvic diseases and, where present, there was invariably blood in the peritoneal cavity, not confined to the pelvis. Voluntary resistance to deep pressure was a very common sign.

Abdominal tenderness was frequently absent in cases of pelvic hematocele; in unruptured tubal pregnancy and in advanced cases, but in patients who had had a recent severe hemorrhage, the abdomen was generally exquisitely tender.

The figures recorded on pelvic tenderness are undoubtedly too low. Certainly in those patients that have been under my observation, there is usually marked tenderness, and, especially when the pelvis is filled with recent clots, there is an even greater degree of tenderness than is found in cases of pelvic abscess. I have seen two cases of unruptured tubal pregnancy in which firm bimanual compression of the mass elicited no complaint or discomfort, but they are very unusual.

### Signs on Physical Examination

| | | |
|---|---|---|
| Shock (extreme) | 15 | |
| Breasts: | | |
| Lactating | 7 | |
| Colostrum present | 46 | (15%) |
| Abdomen: | | |
| Distention | 90 | (30%) |
| Free fluid | 33 | (10%) |
| Mass | 72 | (24%) |
| Tenderness, general | 21 | (7%) |
| Tenderness, limited to lower abdomen | 71 | (23%) |
| Tenderness, limited to lower right quadrant | 52 | (17%) |
| Tenderness, limited to lower left quadrant | 39 | (13%) |
| Muscle spasm | 11 | (4%) |
| Rigidity | 17 | (6%) |
| Pelvis: | | |
| Vaginal cyanosis | 6 | (2%) |
| Bloody discharge from vagina | 85 | (25%) |
| Cervix softened | 85 | (25%) |
| Cervix enlarged | 48 | (16%) |
| Fundus softened | 15 | (5%) |
| Fundus enlarged | 86 | (25%) |
| Mass, boggy | 83 | (24%) |
| Mass, firm | 38 | (12%) |
| Mass, cystic | 40 | (13%) |
| Blood clot crepitus | 21 | (7%) |
| Tenderness | 146 | (48%) |

## HEMOGLOBIN AND LEUCOCYTE COUNT

Unfortunately, hemoglobin determinations and leucocyte counts were not done in many of the cases. It is to be remembered that the lowest point of the hemoglobin curve is not obtained until from 48 to 72 hours after an acute hemorrhage (Dunn & Wynne, John Hopkins Hospital Bulletin, XXIX, No. 323, January, 1918). On this account, the degree of anæmia caused by the acute hemorrhage is not determined as a rule before operation. A high leucocyte count is usually found shortly after acute intraperitoneal hemorrhage and cannot by itself be considered an indication of infection. In our small series of leucocyte counts, there were between 20,000 and 30,000 leucocytes in 8 cases (10%) and between 10,000 and 20,000 in 39 cases (47.5%). This observation agrees with those reported by other authors.

### Hemoglobin Before Operation

| Per cent of hemoglobin | Number of patients | Per cent of hemoglobin | Number of patients |
|---|---|---|---|
| 15 | 1 | 60–70 | 18 |
| 20–30 | 3 | 70–80 | 20 |
| 30–40 | 13 | 80–90 | 16 |
| 40–50 | 7 | 90–100 | 9 |
| 50–60 | 19 | | |

**Total number of patients on whose blood hemoglobin determinations were done prior to operation, 106.**

LEUCOCYTE COUNT BEFORE OPERATION

| W. B. C. | No. of patients | W. B. C. | No. of patients | W. B. C. | No. of patients |
|---|---|---|---|---|---|
| 3,000 | 1 | 10,000–11,000 | 12 | 16,000–17,000 | 3 |
| 5,000–6,000 | 2 | 11,000–12,000 | 1 | 17,000–18,000 | 1 |
| 6,000–7,000 | 6 | 12,000–13,000 | 8 | 18,000–19,000 | 2 |
| 7,000–8,000 | 6 | 13,000–14,000 | 2 | 20,000–21,000 | 1 |
| 8,000–9,000 | 11 | 14,000–15,000 | 4 | 22,000–23,000 | 5 |
| 9,000–10,000 | 9 | 15,000–16,000 | 6 | 30,000– | 2 |

Total number of patients on whom leucocyte counts were made before operation, 82.

## TEMPERATURE AND PULSE

The temperature on admission to the hospital was less than 101° F. in 164 (91%) of a series of 180 consecutive admissions for ectopic gestation and the pulse was less than 130 per minute in the same number of patients. The majority showed some increase in both pulse rate and temperature.

TEMPERATURE AND PULSE ON ADMISSION TO THE HOSPITAL OF 180 CONSECUTIVE PATIENTS

| Temperature | No. of patients | Temperature | No. of patients | Temperature | No. of patients |
|---|---|---|---|---|---|
| Did not register... | 1 | 99.5–100 | 29 | 102.0–102.5 | 5 |
| 97.0–98.0 | 5 | 100.0–100.5 | 30 | 102.5–103 | 0 |
| 98.0–98.5 | 30 | 100.5–101 | 8 | 103.0–103.5 | 1 |
| 98.5–99.0 | 26 | 101.0–101.5 | 5 | 103.5–104 | 2 |
| 99.0–99.5 | 41 | 101.5–102 | 3 | | |

| Pulse | No. of patients | Pulse | No. of patients | Pulse | No. of patients |
|---|---|---|---|---|---|
| 60–70 | 4 | 110–120 | 16 | 150–160 | 0 |
| 70–80 | 9 | 120–130 | 21 | 160–170 | 2 |
| 80–90 | 22 | 130–140 | 7 | 170–180 | 1 |
| 90–100 | 46 | 140–150 | 5 | Could not be counted | 1 |
| 100–110 | 52 | | | | |

## PRE-OPERATIVE DIAGNOSIS

The pre-operative diagnosis was recorded on the history in 212 cases. The correct diagnosis was made on admission in 98 cases (46%) and confirmed on examination after the patients had been anæsthetized for operation. Twelve additional cases were diagnosed correctly only after the patients were under anæsthesia, while a probable diagnosis of extrauterine pregnancy was made in five other cases, one of which had a posterior vaginal coeliotomy performed before the laparotomy for confirmation of the diagnosis. In 28 other cases the condition was suspected but not definitely diagnosed until some operative procedure had been performed. In 69 cases (33%) the extrauterine pregnancy was not diagnosed, although in a number of these cases some other pathological condition present was diagnosed correctly. The diagnoses recorded were made by some member of the resident staff in the large majority of the cases.

TABLE OF DIAGNOSES BEFORE OPERATION

| | |
|---|---|
| Extrauterine pregnancy (on admission examination) | 98 cases |
| Extrauterine pregnancy (on examination under anæsthesia | 12 cases |
| Extrauterine pregnancy (probable diagnosis) | 4 cases |
| Extrauterine pregnancy (after exploratory puncture) | 1 case |
| Retained membranes of extrauterine pregnancy | 11 cases |
| Pelvic abscess or extrauterine pregnancy | 6 cases |
| Chronic pelvic inflammatory disease or extrauterine pregnancy | 6 cases |
| Appendix abscess or extrauterine pregnancy | 1 case |
| Chronic appendicitis or extrauterine pregnancy | 1 case |
| Cystoma of ovary or extrauterine pregnancy | 1 case |
| Myoma uteri or extrauterine pregnancy | 1 case |
| Calcified myoma or lithopedion | 1 case |
| Fibro-cystoma | 1 case |
| Ovarian cyst with twisted pedicle | 1 case |
| Multilocular cystic ovary | 1 case |
| Ovarian tumor | 1 case |
| Ovarian tumor (malignant) | 1 case |
| Papillomatous cyst of ovary | 1 case |
| Parovarian cyst | 1 case |
| Myomata uteri | 5 cases |
| Myomata uteri with pregnancy | 2 cases |
| Myomata uteri, cystic, or sarcoma of uterus | 1 case |
| Myomata uteri, cystic, or angioma of uterus | 1 case |
| Myomata uteri with adherent dermoid cyst | 1 case |
| Pelvic abscess | 11 cases |
| Pelvic abscess with general peritonitis | 1 case |
| Pelvic abscess or appendix abscess | 1 case |
| Chronic pelvic inflammatory disease | 20 cases |
| Subacute pelvic inflammatory disease | 2 cases |
| Acute pelvic inflammatory disease | 1 case |
| Chronic appendicitis | 2 cases |
| General peritonitis | 1 case |
| Retained membranes | 2 cases |
| Abortion, infected | 1 case |
| Miscarriage due to retroposition of the uterus | 1 case |
| Pregnancy | 1 case |
| Retroposition of the uterus | 2 cases |
| Chronic pelvic inflammatory disease, Tubo-ovarian abscess, Ovarian cyst | 1 case |
| Submucous myoma, cystic, Ovarian tumor, Extrauterine pregnancy, Chronic pelvic inflammatory disease | 1 case |
| Papillocystoma of ovaries, Tuberculous pelvic inflammatory disease, Pelvic inflammatory disease with ovarian cyst | 1 case |
| "No diagnosis made" | 3 cases |

We do not believe that the flat-footed diagnosis of extrauterine pregnancy is as simple as many writers consider it. In making an estimate of the percentage of faulty diagnoses, we should also include those cases diagnosed as extrauterine pregnancy which, at operation, prove to be another condition. In this clinic the latter class of cases is numerous. In private practice among more intelligent patients, there should be a higher percentage of correct diagnoses made than in a free clinic. The classical case of an acute ruptured ectopic pregnancy is usually clear if a satisfactory history can be obtained, but there are a great many cases in which the history points equally well to pelvic inflammatory disease. The latter disease also gives symptoms that not infrequently strongly suggest extrauterine pregnancy. Cases with unilateral inflammatory disease are seen in this clinic fully as often as extrauterine pregnancies and may be very puzzling. The

differential diagnosis in this class of cases is often difficult even when a careful history has been taken.

Very often there are other conditions present that make a positive diagnosis practically impossible. Another stumbling-block is encountered occasionally in patients who have had an early abortion with retained membranes and have a cystic ovary on one side. We have seen three cases of this character which were correctly diagnosed by one or more members of the staff, but which were considered to be unruptured extrauterine pregnancies by other members who examined the patients under equally favorable circumstances.

There are occasional cases in which the diagnosis is in doubt even after operation has been performed, as in the following:

Gyn. No. 22180. The patient was a white woman, age 33; she was admitted to the hospital May 16, 1916, complaining of "bowel trouble."

Married 12 years; three children, youngest six years of age. No miscarriages. Labors normal. Fever for two weeks beginning in the fourth week following the first labor; otherwise the puerperia were normal.

Last menstrual period February, 1916; last preceding October, 1915. Miscarriage on January 1, 1916, after slight vaginal bleeding for the preceding week. A curettage was done by her family physician January 2 and the patient was told that "the afterbirth was perfect." No fœtus was seen. A period normal, except slightly prolonged, began on February 7 and lasted seven days. On February 21 an appendectomy and a curettage were performed. The surgeon who operated said that the uterus, tubes and ovaries were normal at that time. No pain followed the operation until April 6, when she had a gradually increasing pain in the lower abdomen and back. This became quite severe, but lasted only one day. The abdomen felt sore for the following three days. She had no further abdominal pain until May 13 at 6 p. m., when she began to have pain in the left lower quadrant of the abdomen, similar to the previous attack. There had been slight vaginal bleeding for three days prior to this attack, during which the bleeding increased considerably. This attack of pain lasted 36 hours.

*P. E.*—Pulse 100. Temperature 99.6°, May 15, 1916. W. B. C., 19,000. Hbg. 95%.

Abdominal tenderness marked in the left lower quadrant and less marked in the right lower quadrant. Moderate rigidity below the umbilicus. A firm, smooth mass can be felt about half way between the umbilicus and pubis.

*Pelvic Examination.*—A bloody vaginal discharge is present. Cervix slightly softened and slightly enlarged. The tumor described above seems to be the uterus. A moderately firm mass, which is tender, can be felt in the left fornix. Blood clot crepitus in the cul-de-sac.

*Diagnosis.*—Extrauterine pregnancy, left, probably with beginning tubal abortion.

*February 17, 1916.*—Operation. A pelvic puncture was performed and about three ounces of old black blood was evacuated from the pelvis. The patient was immediately prepared for laparotomy. There was a considerable amount of old blood in the abdomen. The tubes were found densely adherent in the cul-de-sac, the fimbriated ends were open, both tubes were considerably enlarged and œdematous. No fœtal or placental tissue could be found, nor was there any visible site of an ectopic pregnancy in either tube. The tubes were released from adhesions and a cigarette drain placed through the cul-de-sac. There was a good deal of fresh bleeding during the operation. The patient was discharged June 16 after a rather prolonged convalescence. At the time of discharge the uterus was still enlarged, but there were no pelvic masses or tenderness.

## TREATMENT

The treatment of our cases has been operative, either by the abdominal or vaginal routes. In several cases posterior vaginal coeliotomy has been performed for diagnosis. Pelvic puncture has been employed for pelvic hematocele in a number of cases, although in 60% of these cases a laparotomy was performed immediately afterwards.

### Table of Operations

| | | |
|---|---|---|
| Vaginal (only) | 24 cases | (8%) |
| Pelvic puncture (only) | 16 cases | |
| Pelvic puncture with laparotomy (for hemorrhage following puncture, 4) | 24 cases | |
| Pelvic puncture with dilatation and curettage | 3 cases | |
| Dilatation and curettage with laparotomy | 5 cases | |
| Vaginal salpingectomy | 1 case | |
| Exploratory above Poupart's ligament into sac | 3 cases | |
| Laparotomy | 279 cases | (92%) |
| Abdominal incision of sac with drainage | 5 cases | |
| Removal of fœtus and placenta | 6 cases | |
| Salpingectomy (unilateral) | 180 cases | |
| Salpingectomy (bilateral) | 56 cases | |
| Resection of one tube | 1 case | |
| Puncture of hematosalpinx | 2 cases | |
| Total extirpation of sac and contents | 12 cases | |
| Partial extirpation of sac | 1 case | |
| Oöphorectomy (unilateral) | 108 cases | |
| Oöphorectomy (bilateral) | 24 cases | |
| Resection of one ovary | 11 cases | |
| Ovarian cyst tapped | 1 case | |
| Hysterectomy | 30 cases | |
| Resection of uterine cornu | 7 cases | |
| Myomectomy | 5 cases | |
| Excision of accessory tube | 1 case | |
| Ligation of remaining tube | 1 case | |
| Excision of abscess sac | 1 case | |
| Suspension of uterus | 10 cases | |
| Excision of mesenteric cyst | 1 case | |
| Excision of umbilical hernia | 1 case | |
| Resection of omentum | 1 case | |
| Release of intestinal adhesions | 5 cases | |
| Suture of rectum | 3 cases | |
| Suture of sigmoid | 1 case | |
| Resection of ileum | 3 cases | |
| Lateral anastomosis | 3 cases | |
| Additional: Perineal repair | 6 cases | |
| Additional: Perineal repair with suture of rectal sphincter | 2 cases | |

Laparotomy by the abdominal route has been preferred in all cases except those in which there was a pelvic hematocele with symptoms and signs indicating infection. In such cases, pelvic puncture and drainage is usually a safer procedure, although a secondary laparotomy may be necessary later for continued pain.

The majority of our patients have entered the hospital after examination in the Out-Patient Department and have been operated upon on the day following admission, unless they were in serious condition at the time of admission, when immediate operation has been performed, with very satisfactory results. One patient whose case has been previously reported by Richardson (JOHNS HOPKINS HOSPITAL BULLETIN) was in very extreme shock when admitted to the hospital and was treated expectantly. However, three days later, operation became imperative on account of marked abdominal distention and she died on the third day after the operation. Richardson thought this patient could have been operated upon the day following admission, when she had recovered somewhat from the primary shock and before serious distention had set in.

Whenever other pathological conditions demanding operation were present, they were included in the operative treatment, when the patient's condition justified a prolongation of the procedure.

*Peritoneal Toilet.*—In the majority of our cases the peritoneal cavity had been cleaned of blood and clot as well as possible. In 259 cases the peritoneal cavity was cleaned of blood and clot, and in eight cases no attempt was made to evacuate blood. We believe that the convalescence is more satisfactory when the blood is carefully removed.

*Irrigation.*—The peritoneal cavity was irrigated in 37 cases, sterile normal salt solution being used in 35 cases and sterile water in two cases. In recent years this practice has been discontinued.

The sac has been irrigated following pelvic puncture in nine cases, but this procedure has been abandoned on account of the danger of breaking through the wall and filling the peritoneal cavity with the fluid, as occurred in one case and resulted in a general peritonitis. This patient recovered after a secondary operation for drainage of the abdomen.

*Drainage.*—Primary drainage has been used in 150 cases, glass tubes were employed twice and in the remainder gauze usually in the form of a cigarette drain. The drains are preferably placed through the cul-de-sac into the vagina, rather than through the abdominal wall (38 cases were drained through the abdominal incision). At the present time drains are not employed unless there is some evidence of infection in the pelvis or a general ooze following the release of adhesions.

*Stimulants.*—Salt solution administered subcutaneously is depended upon for stimulation during operation and has been employed in 56 cases. Salt solution by rectum has been used in 13 cases and with equal parts of coffee in four cases. The peritoneal cavity was filled with salt solution before closing the abdomen in 34 cases, but this procedure has been discontinued, as it seems to favor post-operative distention and generally increases the patient's discomfort, as well as spreading infection over the entire abdomen, if any should be present. In the case of one patient with very serious shock, an infusion of normal salt solution was administered through the radial artery and resulted in gangrene of the hand. In a few cases drug stimulants have been used hypodermically, strychnine in 16 cases, digitalis in three cases and brandy and ether in one case.

Transfusion of blood has not been used in any case included in this series. Very satisfactory results, however, have been reported by others who have used both direct and indirect transfusion, but sometimes there is no time to match the bloods of donor and recipient and a severe reaction following the transfusion may be fatal. The majority of these acutely ruptured cases can be stimulated sufficiently with subcutaneous infusions of large quantities of salt solution to tide them over the immediate shock. As all these patients are of ages most favorable for operative risk and as a rule have been in good health prior to the acute onset, they usually will recover if stimulated with salt solution for the first few hours.

Lichtenstein (Muench. Med. Wchnschr., 1915, LXII, 1597) reports eight cases treated by reinjection of the blood found in the patient's abdomen after defibrination and dilution with salt solution 3:2, a procedure open to criticism.

The intravenous injection of 7% acacia in distilled water, filtered and sterilized by boiling, will probably prove to be of great value in those cases in which there is severe shock due to great loss of blood volume (Rous-Wilson, Jour. Am. Med. Assn., January 26, 1918). We have used this preparation in one case in which there was an abundant hemorrhage at operation and severe shock, with gratifying results.

There are, of course, patients in such serious shock when first seen that operation is contra-indicated. In these cases shock must be combated by some of the methods mentioned above, but as soon as the patient is in condition to stand operation, it should not be delayed.

The time consumed in operating is shown in the table for 255 cases.

TABLE SHOWING THE DURATION OF OPERATIONS

| Time | Number of cases | Time | Number of cases | Time | Number of cases |
|---|---|---|---|---|---|
| *min.* | | *hrs. min.* | | *hrs. min.* | |
| 5 | 3 | 45 | 22 | 1 25 | 4 |
| 10 | 6 | 50 | 23 | 1 30 | 4 |
| 15 | 4 | 55 | 14 | 1 40 | 2 |
| 20 | 10 | | 21 | 1 45 | 4 |
| 25 | 14 | 5 | 11 | 1 50 | 2 |
| 30 | 21 | 1 10 | 17 | 1 55 | 2 |
| 35 | 29 | 1 15 | 6 | 2 | 2 |
| 40 | 23 | 1 20 | 8 | 2 10 | 2 |
| | | | | 2 25 | 1 |

**Total, 255 operations.**

All operations consuming less than 20 minutes were pelvic punctures only.

Thirty operators performed 267 operations.

| | | |
|---|---|---|
| One operator performed | 44 operations | |
| One operator performed | 35 operations | |
| One operator performed | 27 operations | |
| One operator performed | 21 operations | |
| One operator performed | 15 operations | |
| Two operators performed | 14 operations | (each) |
| One operator performed | 12 operations | |
| One operator performed | 11 operations | |
| One operator performed | 10 operations | |
| One operator performed | 9 operations | |
| One operator performed | 8 operations | |
| Two operators performed | 6 operations | (each) |
| One operator performed | 5 operations | |
| Four operators performed | 4 operations | (each) |
| One operator performed | 3 operations | |
| Six operators performed | 2 operations | (each) |
| Four operators performed | 1 operation | (each) |

*Anæsthesia.*—In the large majority of these cases, nitrous oxide followed by ether, administered by the open drop method, has been used. Some patients have been given chloroform or ether only, and a few chloroform and ether.

DIAGNOSIS AT OPERATION

| | | |
|---|---|---|
| Ruptured with free blood in peritoneal cavity | 100 | (61%) |
| Ruptured with encapsulated blood in peritoneal cavity | 66 | |
| Tubal abortion with free blood in peritoneal cavity | 38 | (19%) |
| Tubal abortion with encapsulated blood in peritoneal cavity | 13 | |
| Unruptured | 55 | (20%) |
| Total | 272 | |
| Interstitial pregnancy, right | 2[1] | |
| Tubal pregnancy, right | 135 | |
| Tubal pregnancy, left | 131 | |
| Ovarian pregnancy, right | 2[2] | |
| Total | 270 | |

[1] Wynne, J. H. H. Bull. XXIX, No. 324, February, 1918.

[2] Cullen & McAll, Surg., Gyn. & Obst., 1912; Myer & Wynne, to be reported.

In one case the pregnant tube was ruptured during the examination under ether. Active hemorrhage at time of operation occurred in 20 cases.

The peritoneum was noted as blood stained before being opened in 43 cases.

The blood in the peritoneal cavity was designated as fluid in 66, clotted in 24 (infected, three); there were fluid and clots in 55 cases.

The opposite tube was noted to be normal in 15 cases.

The opposite ovary was noted to be normal in 12 cases.

The appendix was described as normal in 31 cases.

The appendix was involved in the sac in 11 cases.

The appendix was adherent to a myoma in one case.

### A CASE OF PREGNANCY IN A RUDIMENTARY HORN

Gyn. No. 16727. The patient was a white woman, age 30, admitted to the hospital June 9, 1910, complaining of vaginal bleeding and pain the left side of the abdomen. Married five years; one child two years old. One miscarriage at two months, one year ago. Labor and puerperia normal. Last menstrual period January, 1910.

*P. I.*—The patient considered herself pregnant, but noticed that the uterus had not enlarged as rapidly as during her former pregnancy and that the enlargement was more on the left side than on the right. For a month she has noticed tenderness over the left side of the abdomen. At 6 a. m. on the morning of admission, she was awakened by pains in the pelvis, similar to labor pains and shortly after, passed blood and bits of tissue resembling placenta. There was slight bleeding afterwards, but the pain subsided. She was nauseated this morning.

*Physical Examination Under Ether.*—On abdominal examination, a mass can be felt in the lower abdomen, which is rather soft and boggy and about the size of a large orange. The mass is movable and seems to be attached to the uterus.

ADVANCED EXTRAUTERINE PREGNANCY

| Gyn. No. | Race | Age of patient | Date | Pre-operative diagnosis | Operation | Placenta | Result | Fœtus |
|---|---|---|---|---|---|---|---|---|
| | | *Years* | | | | | | |
| 114 | B. | 29 | 1890 | Fibrocystoma. | Laparotomy. | Removed. | Died. Shock. | Dead. Male. Length 53 cm. |
| 191 | B. | 28 | 1890 | Abdominal pregnancy (several mos. past term). | Laparotomy. | Removed. | Recovery. | Wt. 2800 grms. Male. Dead. Fully developed. Crown rump 30 cm. |
| 1,795 | W. | 42 | 1893 | Ectopic, two months past term. | Laparotomy. | Removed. | Died. General peritonitis. | Dead. Length, 42 cm.; wt., 4 lbs. |
| 4,564 | B. | 45 | 1896 | Calcified myoma or lithopedion four years past term. | Laparotomy. (Reported by J. G. Clark). | Removed. | Recovery. | Lithopedion. Weight, 4¾ lbs. |
| 7,182 | W. | 34 | 1899 | Multilocular cystoma ovarii. | Laparotomy. | Removed. | Recovery. | Dead. Length, 25 cm. |
| 12,207 | W. | 41 | 1905 | Ruptured tubal pregnancy, two months past term. | Laparotomy. | Removed. | Recovery. | Macerated. Weight, 1250 grms. Dead. |
| 13,272 | B. | 28 | 1906 | ..... | Laparotomy. | Removed. | Recovery. | Full term, female. Living. |
| 13,546 | W. | 35 | 1907 | Extrauterine pregnancy, ruptured. | Laparotomy. | Removed. | Recovery. | Six months, 33 cm. long. |
| 13,673 | B. | 30 | 1907 | ..... | Laparotomy. | Removed. | Recovery. | Intraligamentary, full term. |
| 13,806 | B. | 33 | 1907 | Abdominal pregnancy. (Reported by Cullen, | Laparotomy. Surg., Gyn. & Obst., 1915, XX, 261.) | Removed. | Recovery. | Macerated remains of fœtus. |
| 17,656 | W. | 35 | 1911 | ..... | Laparotomy. | Removed. | Recovery. | Dead. Intraligamentary, rt. Weight, 6½ lbs. |
| 19,092 | B. | 22 | 1913 | Extrauterine pregnancy, infected. | Laparotomy. | Removed. | Died. General peritonitis. | Macerated. Femur, 5.2 cm. Humerus, 4.8 cm. |
| 21,494 | B. | 29 | 1915 | Ovarian tumor, right. | Laparotomy. | Removed. | Recovery. | Dead. Weight, 1911 grms. 44.5 cm. |

*Pelvic Examination.*—The vagina and cervix are normal. The fundus of the uterus is soft and boggy and, attached to it by a pedicle, is the mass described above.

*Pre-Operative Diagnosis.*—Extrauterine pregnancy or pregnancy in a rudimentary horn.

*Operation.*—The mass was found to be a pregnancy in the rudimentary left horn of a bicornate uterus and was attached to the right side of the uterus by a small pedicle. The left tube was stretched over the pregnant horn and together with the left ovary was so intimately associated with it as to necessitate their removal. The left horn was amputated close to the right side and there remained a practically normal uterus.

The patient was discharged on the 13th day after an uncomplicated convalescence.

*Diagnosis.*—Pregnancy in a rudimentary horn, left.

*Pathological No. 15,150.*—The specimen has been opened anteriorly in the operating-room and measures 7 x 8 x 5 centimeters. The walls measure 1.5 centimeter in thickness. Fœtus of 4 to 5 months in unruptured membranes.

### Pathological Reports

The tissues removed at operation have been studied histologically and the diagnosis has been verified. We are unable at the present time to give a thorough report on this interesting side of the disease.

The routine preparations, where the endometrium was examined, have been reported as follows:

| | |
|---|---|
| Normal endometrium | 13 |
| Gland hypertrophy of the endometrium | 5 |
| Endometritis, chronic | 5 |
| Endometritis, acute | 1 |
| Decidual reaction of the endometrium | 7 |
| Cast of uterine cavity with decidual reaction | 2 |

In addition to ectopic pregnancy the following diagnoses were made at or before operation:

| | |
|---|---|
| Atrophy of the opposite tube | 1 |
| Hematosalpinx of the opposite tube | 3 |
| Hydrosalpinx of the opposite tube | 16 |
| Chronic salpingitis of the opposite tube | 8 |
| Pyosalpinx of the opposite tube | 6 |
| Tubo-ovarian abscess of opposite tube | 1 |
| Ovarian abscess | 3 |
| Chronic pelvic inflammatory disease | 92 |
| Cystic ovaries | 13 |
| Ovarian cyst, follicular | 9 |
| Ovarian cyst, corpus luteum | 3 |
| Parovarian cyst | 1 |
| Retroposition of the uterus | 6 |
| Myomata uteri | 17 |
| Membranous dysmenorrhœa | 1 |
| Mesenteric cyst | 1 |
| General peritonitis | 1 |
| Pre-operative rupture of abscess into rectum | 1 |
| Post-operative adhesions | 1 |
| Bladder adhesions | 1 |
| Omental adhesions | 14 |
| Intestinal adhesions | 19 |
| Meckel's diverticulum | 1 |
| Umbilical hernia | 2 |
| Appendicitis, chronic | 52 |
| Appendicitis, sub-acute | 5 |
| Appendicitis, acute | 2 |
| Periappendicitis | 7 |

Complications before operation:

| | |
|---|---|
| Pulmonary tuberculosis | 2 |
| Diabetes | 1 |
| Insanity | 1 |
| Arthritis deformans | 1 |
| Chronic nephritis | 1 |
| Ascaris lumbricoides | 1 |
| Uncinaria Americana | 1 |

### Post-operative Complications

The complications following operations have been as follows:

| | | |
|---|---|---|
| Acute bronchitis | 2 cases with recovery. | |
| Bronchopneumonia | 2 cases with recovery. | |
| Lobar pneumonia | 2 cases with 1 death. | |
| Fecal fistula, abdominal | 2 cases with 1 death | 1 patient. |
| Fecal fistula, vaginal | 1 case with death... | |
| Urinary fistula, abdominal | 1 case with death... | |
| Atonic ileus | 1 case with recovery. | |
| Peritonitis, general | 6 cases with 5 deaths. | |
| Infected drainage cavity with collection of pus | 3 cases with recovery. | |
| Cystitis | 2 cases. | |
| Phlebitis (of left leg) | 3 cases. | |
| Tetanus | 1 case with recovery. (Reported by Casler at Southern Medical Association meeting in 1917.) | |
| Gangrene of the hand following intra-arterial (radial) salt infusion | 1 case. | |
| Mastitis, right | 1 case. | |
| Acute follicular tonsillitis | 1 case. | |
| Influenza | 1 case. | |
| Erysipelas (facial) | 1 case. | |

Shock and anæmia have been omitted from this list, as accurate data for all cases are not available.

### Subsequent Operations for Complications Arising from the Primary Operation

Gyn. No. 2,612. Abdominal drainage for peritonitis following rupture of sac by irrigation after pelvic puncture. Symptoms of peritonitis 11 days after operation. Recovery.

Gyn. No. 7,901. Exploratory laparotomy for localized peritonitis 36 hours after left salpingo-oöphorectomy and vaginal drainage. Death on the sixth day from lobar pneumonia.

Gyn. No. 11,473. Pelvic puncture for drainage, 23 days after salpingo-oöphorectomy. Recovery.

Gyn. No. 11,491. Dilatation of drainage tract and evacuation of pus 10 days after pelvic puncture. Recovery.

Gyn. No. 12,380. Rupture of abdominal incision 22 days after laparotomy. Recovery.

Gyn. No. 15,529. Right salpingo-oöphorectomy and release of adhesions 13 days after pelvic puncture and drainage of infected hematocele. Recovery.

Gyn. No. 17,251. January 16, 1911, at the first operation, during hysterectomy, left salpingo-oöphorectomy and release of adhesions, the rectum was torn. Abdominal fecal fistulæ resulted.

April 29, 1911. Excision of fistulous tracts, suture of rectum and bladder. Appendectomy. Failure.

September 18, 1911. The patient was readmitted to the hospital (Gyn. No. 17,804) for abdominal fecal fistula and a recto-vaginal fistula following her first operation.

September 30, 1911. Excision of abdominal fistula, resection of sigmoid, end-to-end anastomosis, suture of bladder. Shock.

October 5, 1911. Enterostomy for ileus.

October 6, 1911. Enterostomy for ileus. Death on the table.

### CAUSE OF DEATH

There have been 13 deaths in our series of 303 cases and autopsies were performed on six of these.

Gyn. No. 114. (Autopsy No. 72.) Shock 12 hours after operation. This patient was in a very critical condition when operated upon. No anatomical cause of death was found at autopsy.

Gyn. No. 521. (Autopsy No. 181.) Died 24 hours after operation. The anatomical diagnosis at autopsy was: Acute general peritonitis (pure culture *B. coli* from bloody peritoneal fluid), perforation of appendix with circumscribed abscess.

Gyn. No. 1,795. (Autopsy No. 388.) Died 10 days after operation. At autopsy an acute fibro-purulent peritonitis, chronic diffuse nephritis and gallstones were found.

Gyn. No. 7,901. (Autopsy No. 1562.) Death 6 days after operation, of lobar pneumonia.

Gyn. No. 10,678. (No autopsy.) Death 3 days after operation. On admission the hemoglobin was 15 per cent and on the day of death 10 per cent.

Gyn. No. 12,042. (No autopsy.) Death 9 hours after operation. This patient was operated on by the vaginal route and a large amount of clot and fluid blood evacuated, followed by a gush of bright red blood. Laparotomy was immediately performed. Shock.

TABLE SHOWING PREGNANCIES SINCE OPERATION

| Gyn. No. | Character of operation | No. of years since operation | No. of children and miscarriages since operation |
|---|---|---|---|
| 1,636 | Incision of sac with drainage | 24 | 5 full-term children. |
| 1,710 | Enucleation of sac | 24 | 2 full-term children. |
| 2,805 | Right salpingo-oöphorectomy | 23 | 1 full-term child. |
| 4,120 | Pelvic puncture with drainage | 20 | 2 full-term children. |
| 6,482 | Right salpingectomy | 17 | 1 miscarriage at 2½ months 4 years after operation. |
| 8,441 | Right salpingo-oöphorectomy | 15 | 2 full-term children, 1 miscarriage. |
| 9,740 | Left salpingectomy | 14 | 1 miscarriage. |
| 9,746 | Right salpingo-oöphorectomy | 14 | 5 miscarriages, the first 2 years after operation. |
| 10,258 | Left salpingectomy | 14 | 1 full-term child. |
| 10,544 | Left salpingectomy with resection of right ovary | 14 | 2 full-term children. |
| 11,215 | Right salpingo-oöphorectomy | 13 | 2 full-term children. |
| 11,244 | Pelvic puncture and exploratory laparotomy | 13 | 1 full-term child. |
| 11,592 | Right salpingectomy | 13 | 6 full-term children. |
| 11,830 | Pelvic puncture | 12 | 1 tubal pregnancy 8 years after operation. |
| 11,834 | Left salpingo-oöphorectomy | 12 | 1 full-term child. |
| 12,236 | Right salpingo-oöphorectomy | 12 | 2 miscarriages 10 and 8 years ago at 3 months; 1 full-term child 6 years ago. |
| 12,268 | Right salpingectomy | 12 | 1 miscarriage. |
| 12,398 | Right salpingo-oöphorectomy | 12 | 2 miscarriages. |
| 14,167 | Left salpingo-oöphorectomy and resection of right ovary | 10 | 1 full-term child. |
| 15,309 | Left salpingo-oöphorectomy | 8 | 1 full-term child 2 years after operation; 1 miscarriage 6 years after operation. |
| 15,644 | Right salpingo-oöphorectomy | 8 | 1 miscarriage and 1 full-term child 3 years after operation. |
| 15,955 | Left salpingo-oöphorectomy | 7 | 1 full-term child. |
| 17,428 | Right salpingectomy | 5 | 1 full-term child. |
| 18,744 | Right salpingectomy | 4 | 1 full-term child 14 months after operation; 1 full-term child 32 months after operation. |
| 19,781 | Right salpingectomy | 3 | 8 months pregnant when heard from. |
| 20,777 | Resection of right cornu | 2 | 1 full-term child 1½ years after operation. |
| 21,017 | Right salpingectomy, resection of right ovary, myomectomy | 2 | 1 full-term child 1 year after operation. |
| 21,082 | Right salpingectomy | 23 months | 1 miscarriage (induced) 6 months after operation. |
| 21,483 | Right salpingectomy | 20 months | 3 weeks from term when heard from. |
| 22,303 | Right oöphorectomy | 18 months | 1 full-term child 18 months after operation. |
| 22,445 | Left salpingo-oöphorectomy | 16 months | 1 full-term child 11 months after operation. |

FIVE PATIENTS OPERATED ON FOR SECOND ECTOPIC PREGNANCY IN THIS CLINIC

| Gyn. No. | First operation | Second operation | Gyn. No. |
|---|---|---|---|
| 4,147 | Pelvic puncture in 1896 | Right salpingectomy in 1904 | 11,590 |
| 9,781 | Right salpingo-oöphorectomy in 1902 | Left salpingo-oöphorectomy in 1905 | 12,290 |
| 13,776 | Left salpingectomy in 1907 | Right salpingectomy in 1908 | 14,895 |
| 15,771 | Right salpingectomy in May, 1909 | Left salpingectomy in November, 1909 | 16,188 |
| 16,230 | Right salpingo-oöphorectomy in November, 1909 | Hysterectomy; left salpingo-oöphorectomy in January, 1911 | 17,251 |

These six fatalities were reported in Kelly's Operative Gynecology, Vol. II.

Gyn. No. 12,830½. (No autopsy.) Death 4 hours after operation. The patient was in serious shock when operated upon. About 2 liters of free blood were evacuated from the abdomen.

Gyn. No. 15,314. (No autopsy.) Death 3 days after operation from shock. (Reported by E. H. Richardson.)

Gyn. No. 17,119. (No autopsy.) Death 2½ hours after operation. The patient was in good condition after the operation until 3 minutes before death. Probably embolus.

Gyn. No. 17,211. (Autopsy No. 3489.) Death 8 days after operation. Anatomical diagnosis at autopsy: Acute general peritonitis.

Gyn. No. 17,251. (No autopsy.) Death 8 days after secondary operation for fistulæ following primary operation. General peritonitis.

Gyn. No. 18,731. (No autopsy.) Death 2½ hours after operation. Shock. This patient had diabetes.

Gyn. No. 19,092. (Autopsy No. 3884.) Death 12 days after operation. At autopsy acute general peritonitis and embolic pneumonia were found. At operation the sac containing fœtal bones and infected material was ruptured.

### IMMEDIATE RESULTS

| | | |
|---|---|---|
| Well | 271 | (89.4%) |
| Improved | 19 | (6.3%) |
| Died | 13 | (4.3%) |

### ULTIMATE RESULTS

Letters were sent to the 290 patients who recovered from the operations for ectopic pregnancy. Answers to the follow-up letters were obtained from 118 patients and nine, who did not answer the letter, were later readmitted to this hospital. Of 120 patients, 100 have been well since operation, five have had poor health since operation, seven report fair health and two no change in general health since operation. Four had good health for several months or years, and afterwards died, one of pulmonary tuberculosis, one of acute intestinal obstruction, one of post-operative pneumonia. In one case the cause of death was not stated.

Of the series of 127 cases, there was no possibility of future pregnancy in 33. Of the remaining 96 in whom there was a possibility of future pregnancy 36 (38°) have since become pregnant one or more times; 61 pregnancies have resulted in 37 full-term children; two patients were pregnant almost at term when heard from. In 16 cases the pregnancy ended in miscarriages and six patients had a second extrauterine pregnancy.

### OPERATIONS SUBSEQUENT TO OPERATION FOR ECTOPIC PREGNANCY

Post-operative ventral hernia has occurred in eight cases; four have been repaired in this hospital and one in another hospital, and three patients have not been submitted to another operation. One patient was operated upon for intestinal obstruction and one had a vaginal panhysterectomy performed in this hospital for carcinoma of the cervix.

In all 145 patients have been followed on this point.

I wish to thank Dr. Howard A. Kelly for permission to publish this report.

# NOTES AND NEWS

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